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SOME POSSIBILITIES FOR MEASURING SELECTION INTENSITIES IN MAN[1]*

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IT is convenient to consider selection intensity at three levels—total, phenotypic, and genotypic.

There can be selection only if, through differential survival and fertility, individuals of one generation are differentially represented by progeny in succeeding generations. The extent to which this occurs is a measure of *total* selection intensity. It sets an upper limit on the amount of genetically effective selection.

Not all the differential can be associated with differences in phenotype, for there are large environmental and random elements in survival and reproduction. But, to the extent that differences can be associated with phenotype, *phenotypic* selection intensity can be measured.

Selection can be genetically effective only if it is *genotypic*, that is, if different genotypes make differential contributions to future genera-

[1] Paper No. 660 from the Department of Genetics. I should like to acknowledge the help received in numerous discussions with Dr. Newton Morton and Dr. Ove Frydenberg.

* The first four articles in this issue were read before the Wenner-Gren Supper Conference on Natural Selection in Man, held at the University of Michigan on 12 April 1957. These papers are also being published as *Memoir No. 86* of the American Anthropological Association and also as a hard cover book, *Natural Selection in Man*, by the Wayne State University Press.

tions. Thus natural selection is an inefficient process with only a fraction, perhaps a small fraction, of mortality and fertility differences being genetically effective. Furthermore, very little of the genotypic selection effects any permanent biological improvement. As many authors have pointed out (see especially Haldane, '54a), most of the selection is devoted to eliminating recurrent harmful mutants, maintaining systems of balanced polymorphism, and adjusting to momentary fluctuations in the environment—in other words, to maintaining the status quo. Selection is a necessary but not sufficient condition for the directional change of gene frequencies on which evolution depends.

The Total Selection Intensity [2]

The total selection that can occur in man is limited by his low reproductive rate, yet there is still room for fairly intense selection. The most fertile human populations produce 10 or more children per family. This means that if four-fifths of the children were to die prematurely the population number could still be maintained.

I suggest that the total amount of selection is best measured by the ratio of the variance in progeny number to the square of the mean number. (The parents and offspring are assumed to be counted at the same age, perhaps at birth.) This sets an upper limit on the amount of gene frequency change that selection can effect. The reason for the choice of this measure will now be developed.

I shall use *fitness* in a strictly Darwinian sense as the expected number of progeny, counted at the same age as the parents (Fisher, '30). In a precise theoretical analysis of populations, such as man, with overlapping generations it would be better to measure fitness as the natural logarithm of the progeny number, the Malthusian parameter of Fisher ('30: 25). But the cruder formulation is satisfactory for most purposes.

Suppose that the parental generation is counted at birth and consists of a fraction p_1 of individuals with fitness w_1, p_2 with fitness w_2, and so on ($p_1 + p_2 + p_3 + \cdots = 1$). The average fitness of the population is given by

$$\bar{w} = \frac{\sum p_i w_i}{\sum p_i} = \sum p_i w_i.$$

Because of differential productivity, the expected frequency of type

[2] This section has been greatly expanded since the oral presentation as a result of a suggestion of Dr. J. V. Neel, for which I am indeed grateful.

i next generation will be $p_i w_i$, assuming the complete heritability and constancy of fitness. The average fitness next generation will then be

$$\frac{\sum (p_i w_i) w_i}{\sum p_i w_i} = \frac{\sum p_i w_i^2}{\bar{w}}.$$

The relative increment in fitness between the two generations is

$$\frac{\Delta \bar{w}}{\bar{w}} = \frac{\sum p_i w_i^2 - \bar{w}^2}{\bar{w}^2} = \frac{V}{\bar{w}^2} = I \qquad (1)$$

where V is the variance in fitness, and I will be called the *Index of Total Selection.*

This means that if fitness is completely heritable, that is, if each offspring has exactly the average of his parents' fitnesses, the fitness of the population will increase at rate I. A trait or a gene that is genetically correlated with fitness will increase in proportion to this correlation. The index therefore provides an upper limit to the rate of change by selection. The actual change in a character will depend also on its heritability and correlation with fitness.

It is of interest to separate I into two components, associated with mortality and differential fertility. This can be done as follows:

Assume p_d parents (counted at birth) die prematurely, and p_s survive until the child bearing period and have varying numbers of births $(p_s + p_d = 1)$.

		births (x)	
Premature deaths	p_d	0	$\sum_s p_i = p_s$
Survivals	p_s p_0	0	$\bar{x}$ = overall mean number of births
	p_1	1	
	p_2	2	$\bar{x}_s$ = mean number of births per surviving parent
	p_n	n	$p_s = \bar{x}/\bar{x}_s$.

The index I, is defined as $V/\bar{x}^2$, where V is the variance in the number of progeny per parent (counting the non-survivors as leaving 0 descendants).

$$I = \frac{V}{\bar{x}^2} = \frac{1}{\bar{x}^2}\left[p_d(0-\bar{x})^2 + \sum_s p_i(x_i - \bar{x})^2\right]$$
$$= \frac{1}{\bar{x}^2}\left[p_d(0-\bar{x})^2 + p_s(\bar{x}_s - \bar{x})^2 + \sum_s p_i(x_i - \bar{x})^2 - p_s(\bar{x}_s - \bar{x})^2\right]. \qquad (2)$$

Now, let V_m be the variance due to differential mortality and V_f be that due to differential fertility.

$$V_m = p_d(0 - \bar{x})^2 + p_s(\bar{x}_s - \bar{x})^2 = \bar{x}^2 p_d/p_s \tag{3}$$

$$V_f = \frac{1}{p_s}\sum_s p_i(x_i - \bar{x}_s)^2 = \frac{1}{p_s}[\sum_s p_i(x_i - \bar{x})^2 - p_s(\bar{x}_s - \bar{x})^2] \tag{4}$$

thus, from (2), (3) and (4)

$$I = \frac{V_m}{\bar{x}^2} + p_s\frac{V_f}{\bar{x}^2} = \frac{V_m}{\bar{x}^2} + \frac{1}{p_s}\frac{V_f}{\bar{x}_s^2} = I_m + \frac{1}{p_s}I_f \tag{5}$$

where

$$I_m (= V_m/\bar{x}^2 = p_d/p_s) \text{ and } I_f (= V_f/\bar{x}_s^2)$$

are the indices of total selection due respectively to mortality and fertility. The index due to mortality is especially simple, being the ratio of deaths to survivors.

Some numerical examples based on U. S. Census data are given in table 1. The 1950 and 1910 birth distributions are based on the total children ever born to all women who were of age 45-49 in the census year. The variance is somewhat uncertain because the Census reports lump several classes in the high birth numbers, but this is not likely to introduce a very large error. Another source of error is that no allowance was made for women who died during the childbearing period after having one or more children. It was thought better not to attempt such a correction, since there is almost certainly some lack of independence between fertility and mortality in these ages, and any correction based on an assumed independence might make matters worse. However, the error due to neglecting this correction is not likely to be large, for the death rates at these ages are very low, especially in recent years.

The three mortality values in table 1 are chosen to correspond roughly to the total mortality of women from birth to the end of the child bearing period for three time intervals: at present (10%), during the lifetime of women who were 45-49 in 1950 (30%), and during that of women who were 45-49 in 1910 (50%). Thus the most relevant comparison is between rows (2) and (6). During this 40 year period the index of total selection dropped from 2.6 to 2.1, or by about 20%.

It is interesting to note that the component of selection due to differential fertility actually increased during this period. Although the mean number of children per woman (including unmarried) dropped from 3.9 to 2.3, the index of selection due to fertility differences increased almost [illegible]%. Despite a great lowering of fertility rates the pattern of marriages and births was such as to increase the effective fertility differential.

TABLE 1

The total intensity of selection, I, and its components for several hypothetical populations based on U. S. Census data

						I_m	I_f	I_f/p_s	I
(1)	1950	birth	distribution,	10%	mortality	.111	1.143	1.270	1.381
(2)		"	"	30%	"	.429	1.143	1.633	2.062
(3)		"	"	50%	"	1.000	1.143	2.286	3.286
(4)	1910	"	"	10%	"	.111	.784	.871	.982
(5)		"	"	30%	"	.429	.784	1.120	1.549
(6)		"	"	50%	"	1.000	.784	1.568	2.568

The first column, I_m, is the selection intensity due to mortality, the second column, I_f, is that due to differential fertility, and the last gives the total selection intensity from both causes. The third column gives the ratio of I_f to p_s, the fraction of survivors.

The column I_m shows what the selective index would be if premature mortality were the only differential factor, *i. e.*, if all surviving women had the same number of children. This shows that with recent low death rates, differential post-natal mortality provides only a small part of the total opportunity for selection.

Measuring Phenotypic Selection Intensity

Haldane ('54b) has suggested a way of measuring phenotypic selection, and has used human birth weight as an example. He notes that infants of intermediate weight are more likely to survive the hazards of birth and early infancy than those at either extreme. Suppose that of those with the optimum weight a fraction s_o survive, whereas the overall survival is $\bar{s}$. Haldane defines the intensity of natural selection for birth weight as roughly $s_o - \bar{s}$, or more precisely, $\log_e(s_o/\bar{s})$. For example, where s_o is .983 and $\bar{s}$ is .959, the intensity of selection is $\log_e (.983/.959) = .024$. By Haldane's method, the intensity of selection for any quantitative phenotypic effect can in principle be measured. Since the subject is fully discussed in Haldane's paper, I shall say no more here.

Genotypic Selection Intensity: The Genetic Load of a Population

I should like to define as the *load* of a population the extent to which it is impaired by the fact that not all individuals in the population ar-

of the optimum type. In the example above, the average survival is decreased by .024 from what it would be if all infants were of optimum weight.

What I wish to emphasize is the part of the population load that is due to genetic differences. The *genetic load* of a population is defined as the proportion by which the population fitness (or whatever other trait is being considered) is decreased in comparison with an optimum genotype.[3] Thus, if the character being measured is fitness, the genetic load is a measure of the total genotypic selection intensity.

The genetic load has many possible components of which I shall enumerate three that seem to me to be important and possibly amenable to study. For definiteness the discussion will be restricted to death rates, though other components of total selection intensity could in principle be studied this way.

1. *The mutation load.* Part, perhaps a large fraction, of the selection occurring in a population is directed toward the elimination of recurrent harmful mutants. The proportion by which the population fitness is thereby lowered is the mutational load.

2. *The segregation load.*[4] The optimum genotype might not be fixable. The simplest, and I suspect, most important example is a locus with a heterozygote favored over either homozygote with the population thus maintaining a balanced polymorphism. Inferior homozygotes are produced by segregation each generation, lowering the average population fitness and thereby creating a load.

The mutation and segregation loads, though difficult to separate in practice, are quite distinct in principle. Since mutation provides the raw material for evolution, the mutation load is, as Haldane ('37) notes, the price the species pays for the privilege of evolution. This load is

[3] It is quite likely that the optimum population is not made up of a single genotype, but of a variety. For example a society with division of labor would imply a heterogeneous optimum population. However, this possibility does not greatly change the essential problem, if one assumes that within each subset (*e. g.* males and females) there is an optimum genotype.

[4] Dobzhansky ('55, '57) has classified genetic loads into mutational and balanced. My segregation load is a part of his balanced load, since the latter also includes other possible types of polymorphism, *e. g.*, those due to factors that are favored in different niches, or are frequency-dependent. These latter types may not depend on segregation, and the method of analysis would be different.

independent of the system of heredity and would, for example, be the same in asexual as in sexual species. On the contrary, the segregation load could occur only in sexual species since it depends on Mendelian segregation.

3. *The incompatibility load.* This load comes not from the deficiency of any genotype itself, but from the fact that some genotypes have a reduced fitness with certain parents. For example, a zygote of blood group A seems to have a better chance of surviving if its mother is group A rather than group O. Such incompatibilities may possibly account for a substantial fraction of human embryonic deaths. Thus far, these are known only for serological characters, though later research may reveal other possibilities. I shall not discuss this topic further, since it is the subject of Levine's paper later in this symposium.

The Mutational Load

A quantitative assessment of the mutational load may be made by using a principle first discovered by Haldane ('37). Suppose the three genotypes AA, AA', and $A'A'$ survive and reproduce in the ratio $1:1-hs:1-s$.

Genotype	AA	AA'	$A'A'$
Frequency	p^2	$2pq$	q^2
Relative fitness	1	$1-hs$	$1-s$

Unless h is very small, the frequency of the gene A' in the population will be determined almost entirely by the fitness of the heterozygous class, for the homozygotes $A'A'$ will be so rare as to make only a tiny contribution to the selective pressure. Thus, we can ignore the $A'A'$ class and assume the population to be made up only of AA and AA' with negligible loss in accuracy. Every generation the AA' class will be reduced by a fraction hs because of selection, and at equilibrium this will be balanced by new mutations from AA to AA'. This leads to the equation:

$$(2pq)(hs) = m, \text{ or } 2pq = m/hs \qquad (6)$$

where m is the mutation rate. This is the rate for both A genes or twice the rate per gene.

The mutational load, L_m, may be computed as follows. If there were no mutations the population would eventually consist only of AA genotypes with relative fitness 1. But the equilibrium population when mutation

occurs consists of a fraction $2pq$ of AA' types, each of which lowers the fitness by hs. The total proportion by which the fitness is reduced, or the mutational load, then is

$$L_m = (2pq)(hs) = (m/hs)(hs) = m. \qquad (7)$$

This illustrates the principle, which Haldane ('37) showed with less restricted assumptions, that the fitness of a population is lowered as a result of recurrent harmful mutations at a locus by a fraction equal to the mutation rate at that locus. The mutation rate, m, means the total rate for both members of a gene pair.

The significant point is that this is independent of the values of h and s, unless they are very small. If the mutations act independently, the total load becomes the total mutation rate for all loci. If h approaches 0, *i. e.* if the A' gene becomes completely recessive, the load becomes only half as large (since each death or failure to reproduce in a homozygote removes two deleterious genes). But there is reason to think from Drosophila data, and also from direct studies of a few genes in man (Muller, '50), that most " recessive " genes have enough of an effect in the heterozygous state that for the purposes of this analysis they may be treated as dominants.

The Segregation Load

I shall consider as the simplest example of a situation which leads to a segregation load a single locus where the heterozygote is favored over either homozygote.

Genotype	AA	AA'	$A'A'$
Frequency	p^2	$2pq$	q^2
Relative fitness	$1-s$	1	$1-t$

Such a population reaches a stable equilibrium determined by the relative values of s and t. In such a system, if s and t are large in comparison with the mutation rates, which is usually the case, mutation may safely be ignored. The equilibrium frequencies can be easily deduced by the following argument. For a more direct algebraic treatment see Wright ('31) or Fisher ('30: 100).

Each generation a number of A genes proportional to sp^2 is eliminated because of the reduced fitness of the AA genotype. Likewise, a number of A' genes proportional to tq^2 is eliminated because of the inferior

fitness of the $A'A'$ type. Whenever the eliminated proportion of both kinds of genes is the same, their ratio will not change, and the population will be in equilibrium. Thus, at equilibrium

$$\frac{p^2s}{p} = \frac{q^2t}{q}, \text{ or } \frac{p}{q} = \frac{t}{s}, \qquad p = \frac{t}{s+t}, \; q = \frac{s}{s+t}. \tag{8}$$

The proportion by which the average fitness of the population is reduced, in comparison with a hypothetical population composed of AA' heterozygotes, is given by $sp^2 + tq^2$. If we substitute the equilibrium values of p and q into this, we get for the segregation load

$$L_s = sp^2 + tq^2 = st/(s+t). \tag{9}$$

Note that since s and t are ordinarily much larger than m—perhaps as much as two orders of magnitude in a typical case—the segregation load for a particular locus is much larger than the mutation load. But at the same time there must be many more loci of the type leading to a mutational load than those leading to a segregational, so that it is not possible from these considerations to say which has the greater total effect.

Separating the Mutation and Segregation Loads

In a human population these loads are usually indistinguishable. But there are two procedures which may enable some sort of separation of the two factors and make it possible to assess crudely their relative magnitude. The first depends on their differential response to inbreeding. The other is that the relative value of parent-offspring and sib correlations would be expected to be different for the two kinds of loads. These possibilities will now be briefly explored.

Consider a locus that is contributing to the mutational load, and assume that by some process the population is made completely homozygous but the gene frequencies stay the same as before. The population will then be composed of a fraction p of AA homozygotes and q of $A'A'$. Now, if p is nearly one, $2pq$ is almost twice the value of q. Therefore, by equation (6) q is approximately $m/2hs$. The load in such a hypothetical population is qs, or $m/2h$. Since the genetic load of such a locus in a randomly mating population is m, the ratio of the inbred load to the randomly mating load is $1/2h$. This principle has been used to provide an indirect measure of human mutation rates (Morton, Crow and Muller, '56).

Fortunately this ratio depends only on h, the amount of dominance, and not on s. There is no human information on h that is quantitatively reliable, but there is some information from Drosophila lethals and semilethals that h is about .02 (Morton, Crow and Muller, '56).[5] If this value holds for man, we should expect that the number of deaths in a completely inbred population would be about 25 times as great as for the corresponding category in a randomly mating population, or more if there is an appreciable fraction of complete recessives.

The situation is quite different for a locus where the polymorphism is maintained by the superior fitness of a heterozygote. In this case, if the population is made homozygous, the load becomes $sp + tq$. Substituting from (8) leads to a value of $2st/(s + t)$. Thus for a locus with a superior heterozygote, the segregational load is exactly twice as great in a homozygous population as in a randomly mating one.

If there are multiple alleles, the situation with the mutational load is unchanged; the value of m is simply the sum of the mutation rates to all mutant alleles. With the segregation load, multiple alleles complicate the relation.

Consider k alleles at a locus where all heterozygotes are equal in fitness and superior to any homozygote. If the homozygote A_iA_i is selectively inferior by a fraction s_i to the heterozygote, equilibrium is reached when $q_i = 1/s_i \sum(1/s_i)$ (Wright, '49: 372).

The load in a randomly mating population is $\sum s_i q_i^2 = 1/\sum(1/s_i)$. In a homozygous population the load is $\sum s_i q_i = k/\sum(1/s_i)$, or k times as great. When one heterozygote is more fit than the others, the ratio is less than k.

Therefore, unless the segregation load is based on loci with a large number of alleles, maintained in balanced polymorphism, it is not changed very much by inbreeding. In general, I would conclude that if the fitness is greatly decreased by inbreeding it is to that extent largely attributable to the mutation load rather than the segregational. This gives a possible basis for separation of the two.

[5] The reader may be puzzled as to why this value of 2% is taken when most published data on dominance in Drosophila give the value as 4-5%. The reason is that for this purpose we want h for mutants in a natural population. Since those mutants with the largest h values are most rapidly eliminated, those remaining have a smaller average value of h. Recent unpublished results of Hiraizumi give a value of .024.

It is of course impossible to study completely homozygous humans. But it is possible by studying the children of consanguineous marriages of various degrees to infer what would happen with complete homozygosity. For example, one-sixteenth of the genes of the child of a cousin marriage are made homozygous as a consequence of the inbreeding, so the effect of complete homozygosity would be 16 times as great. Calculations (Morton, Crow and Muller, '56) based on the death rates of children from consanguineous marriages in rural France indicate that, whereas the average child from unrelated parents had a probability of about .12 of death between birth and sexual maturity, a complete homozygote would have the equivalent of about 2 lethal genes. Thus the inbreeding load is about 17 times as great as the random load. I conclude therefore that inbreeding effects are due largely to "ordinary" gene loci and not those maintained in polymorphic balance.

If we take the inbred load (assuming it to be entirely mutational in origin) and multiply by $2h$ we can estimate the mutational load in a randomly mating population. In this case the estimate is $2 \times .04$, or .08. This suggests that in this population .08 out of the total death rate of .12 is mutational in origin, which implies that at least $\frac{.08}{.12} = \frac{2}{3}$ of the deaths are genetically selective. However, the data are not very accurate and no one knows how well the average dominance agrees in Drosophila and man. But to the extent that the method and data can be trusted, it would appear that a substantial fraction of deaths between birth (including stillbirths) and sexual maturity owe their ultimate origin to mutation.

While on the subject of death rates of children of consanguineous marriages, I should like to call attention to the importance of measuring death rates in inbred individuals from primitive populations. The difference between consanguineous and non-consanguineous death and fertility rates in different populations would give a basis for assessing selection that is genetic in origin.

A second possibility for distinguishing between these two kinds of loads depends again on Haldane. Haldane ('49) noted that with a heterotic locus the parent offspring correlation in fitness is zero when the population is at equilibrium. On the other hand the sib correlation is high, approaching .5 for small values of s and t. The situation is quite different for a rare dominant factor. (For this purpose a "recessive" mutant having as much as 2% heterozygous effect would behave as a

dominant in population dynamics.) In that case the parent-offspring and sib correlations would be about the same, approaching 0.5. Therefore, the extent to which the parent-offspring correlations in fitness agree with the sib correlations may be a measure of the extent of the mutational load in the populations.

This is much easier to discuss than it is to measure, largely for two reasons. First, these statements hold only for total fitness and not necessarily for its component parts. This would be especially troublesome, as Haldane points out, if there were a negative correlation between fitness components as, for example, if a low childhood survival rate were associated with high adult fertility. The other difficulty is separating genetic effects from environmental. A seemingly lower parent-offspring than sib correlation may mean only that the environments of the sibs are more similar. This might possibly be circumvented by using half sibs in place of parent-offspring correlations, if groups of full and half sibs in the same family could be found. Thus far the method does not appear too promising, but it offers some possibility.

Effect of a Changing Environment

Probably many genes are deleterious in any environment that is likely to be encountered, and others are uniformly beneficial. For such loci, environmental changes make relatively little difference. In contrast to these are genes or genotypes whose selective values are reversed with a change in the environment. It might at first appear that a change of environment that makes one genotype less favored while making another compensatingly more favored would not alter the average fitness of the population, but this is not so. The population is always worse off as a result of the change. The reason is that the newly advantageous genotype, not having had the benefit of increase by natural selection in the past, is rare, whereas the previously favored type is common.

Shifts of environment that cause such reversals of many loci place a load on the population that may be of considerable magnitude, and analogous to the mutational and segregational loads, though requiring different methods of approach.

SUMMARY

Selection intensity may be measured at three levels—total, phenotypic, and genotypic.

An *Index of Total Selection* is proposed, given by the ratio of the variance in number of progeny per parent to the square of the mean

number. The parents and offspring are assumed to be counted at the same age (say, at birth) and those that die before reproducing are regarded as having zero progeny. The index may be separated into components associated with mortality and differential fertility. Applied to U. S. Census data, the change from 1910 to 1950 was to a decreased opportunity for selection by mortality, but an increase in that due to differential birth rates.

Phenotypic selection is briefly discussed, using a procedure of Haldane's ('54b).

Genotypic selection is measured in terms of the *genetic load*, the extent to which the population is impaired by recurrent mutation (mutational load), by segregation from unfixable superior genotypes (segregation load), and by parental-child incompatibilities (incompatibility load) The mutation load is strictly proportional to the mutation rate, while the segregation load is almost independent of it. The mutation load is particularly sensitive to inbreeding, so the study of children of consanguineous marriages provides an opportunity for its measurement.

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THE INFLUENCE OF THE ABO SYSTEM ON Rh HEMOLYTIC DISEASE [1]

BY PHILIP LEVINE

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IN the remarkable example of selection against the heterozygote Rh positive (*Dd*) infant suffering from hemolytic disease, one gene *D* and one gene *d* are eliminated in all fatal cases and in all surviving infants suffering the complications of kernicterus. With an incidence of genes *D* and *d* as 60 and 40% respectively in a Caucasoid population, there is a more rapid diminution of the less frequent gene *d*. It was quickly pointed out by Fisher *et al.* ('44) and Spencer ('47) that in families with loss through hemolytic disease there is a tendency to compensate by a larger number of pregnancies on the part of the Rh sensitized woman. This was shown by Glass ('50) to be true at least for his white population but not for Negroes, largely because of the larger number of pregnancies and larger number of surviving children per family in the latter group. In any event, compensation results in the survival of normal Rh negative (*dd*) and therefore unaffected infants if the husband is heterozygous. With each surviving child, two *d* genes are added to the population, and it is conceivable that for the white population the end result might actually be overcompensation. Even with homozygous husbands, an ever increasing number of severely affected infants are now salvaged.

This paper will deal with the various factors involved which play an important role in this example of selection against heterozygotes—those

[1] The author wishes to acknowledge the help of Dr. Blandine Y. Gosselin in preparing the tables and the bibliography.

which may be classified as interfering with nature's experiment but particularly with the influence of ABO blood group systems.

A few remarks may be made regarding the incidence of hemolytic disease in general. In the first place, the incidence is directly dependent upon the number of Rh negative individuals in any given population (Levine, '42). Thus, Rh hemolytic disease is exceedingly rare in all populations that are almost exclusively Rh positive, such as Chinese, Japanese, and Amerindians. It is two to three times more frequent in white (15% Rh negative) than in Negroes (5 to 6% Rh negative). It should be more frequent in Basques who are characterized by 30% of Rh negatives, but a protective factor is the proportionately lower incidence of homozygote fathers. In a Caucasoid population the total incidence of Rh hemolytic disease is about one out of 150 full-term pregnancies. An important factor responsible for this comparatively high incidence of hemolytic disease was the random transfusions of the female population without taking into account the Rh differences (Levine and Waller, '46). With current and future transfusions of Rh negative girls and women exclusively with Rh negative blood, the incidence, particularly of severe and fatal cases, will be reduced to a considerable degree. Another factor interfering with nature's experiment of selection against the heterozygote is the successful therapy of severely affected infants and the almost complete reduction of kernicterus to its vanishing point (Hsia, Allen, Gellis and Diamond, '52).

Of all cases of hemolytic disease, about 12 to 15% end in stillbirths or hydrops with death shortly after birth (Walker and Murray '56). There is as yet no single therapeutic measure which will prevent stillbirths due to hemolytic disease. However, their incidence may be diminished somewhat if isoimmunization by random transfusions can be prevented so that the family is completed before stillbirths can manifest themselves.

The bulk of hemolytic disease is contributed by a comparatively small group of Rh negative women, but until recently there were no systematic studies to determine which of the Rh negative women would be capable of producing antibodies. In 1954, Owen, *et al.* invoked the phenomenon of acquired tolerance in order to explain the individual variations in the capacity of producing antibodies, advancing some evidence to indicate that Rh negative sensitized women were more likely to have Rh negative mothers than Rh positive mothers. The assumption was that in a pregnancy of an Rh positive mother with an Rh negative fetus, the latter is

exposed to maternal Rh antigens and therefore will fail to produce antibodies as a result of acquired tolerance, just as in case of the multiple birth in cattle due to in-utero exchange of intact cells (Owen '45). This concept, however, failed to apply to a group of sensitized mothers who gave birth to infants with hemolytic disease, and similar negative results were previously reported by Booth, *et al.* ('53) in a series of 113 affected infants.

TABLE 1

The Possible Role of Acquired Tolerance

Rh STATUS OF THE Rh NEGATIVE MOTHER'S MOTHER

		Positive	Negative
No antibodies	(Owen, *et al.* 1954)	25	9
Antibodies	" " " "	3	14
Hemolytic Disease	" " " "	14	7
Hemolytic Disease	(Booth, *et al.*, 1953)	67	46

The concept of acquired tolerance in relationship to the facility of antibody production with subsequent hemolytic disease is indeed a fascinating one and requires a comprehensive systematic survey. But such studies must take into account the effect of ABO blood group compatibility or incompatibility as first pointed out by the writer in 1943 and amply confirmed by numerous investigators. A compatible mating may be defined as one in which the wife's serum if containing anti-A and/or anti-B will fail to react with her husband's red cells, while in an incompatible mating her serum will agglutinate her husband's red cells.

The original findings on the effect of ABO incompatibility in Rh sensitization and those in additional studies based on the largest number of matings are given in table 2.

In all series there is a lower incidence of ABO incompatible matings varying from 13 to 19.5% in the studies carried out after 1943 when more accurate criteria were available for selection of the cases. In the 3 series in which mothers previously transfused were excluded—those of Malone ('49), Donohue, *et al.* ('54), and Walsh and Kooptzoff ('54)—the values were 19, 18.4 and 14.8% respectively.

The author's series of 501 matings of husband and Rh negative sensitized wife are listed in table 3 as ABO compatible and ABO incompatible. In each case the blood group of the Rh positive husband is given first.

TABLE 2

MATINGS OF Rh POSITIVE HUSBANDS AND Rh NEGATIVE MOTHERS WITH AFFECTFD INFANTS

Author	Number of Matings	ABO Compatible	ABO Incompatible
Levine ('43)	random matings [a]	65	35
Donohue, *et al.* ('54)	random matings [b]	66.5	33.5
Levine ('43)	215	75.3	24.7
Van Loghem and Spaander ('48)	240	87	13
Wiener, Wexler, and Hurst ('49)	282	82.2	17.8
Malone [c] ('49)	373	81	19
Heisto [d] ('55)	507	81.5	18.5
Stratton ('53)	319	83	17
Donohue, *et al.* [c] ('54)	481	81.6	18.4
Race ('54)	247	84	16
Walsh and Kooptzoff [c] ('54)	216	85.2	14.8
Reepmaker ('55)	1742	81.5	18.5
Stern, *et al.* ('56)	238	87	13
Levine—present study	501	80.8	19.2

a. Based on an incidence of the following: group O 45%; group A 41%; group B 10%; group AB 4%.

b. Based on ABO grouping of 1,000 children over 6 months of age in the Hospital for Sick Children, Toronto.

c. Mothers giving histories of previous transfusions were excluded. In other studies no mention was made of transfused mothers. Such mothers were not excluded in the author's series of 1943 or 1954.

d. The incidence of group A in this series is 50.6 in contrast to 40% in other caucasoid populations (see table 6). The value of 18.5% incompatible matings in this population is to be compared with 40% incompatible random matings. This series includes most of the 185 matings previously reported by Brendomoen ('52), who reported 14% ABO incompatible combinations.

TABLE 3

THE 501 MATINGS WITH Rh NEGATIVE MOTHERS OF Rh AFFECTED INFANTS

ABO Compatible		ABO Incompatible	
♂ ♀		♂ ♀	
O × O	133		
O × A	117	A × O	57
O × B	27	B × O	19
O × AB	10	AB × O	0
A × A	100		
A × AB	6	AB × A	3
B × B	6		
B × AB	5	AB × B	1
AB × AB	1		
		A × B	5
		B × A	11
Total	405		96
Percent	80.8		19.2

TABLE 4

ABO RECIPROCAL MATINGS IN Rh HEMOLYTIC DISEASE

Selected From a Total of 3,123 Matings

	COMPATIBLE							INCOMPATIBLE					
♂ ♀	M *	R	H	L	Total Observed	Total Expected	♂ ♀	M	R	H	L	Total Observed	Total Expected
O × A	102	435	111	117	765	*764.0*	A × O	41	172	49	57	319	*320.0*
O × B	17	91	21	27	156	*167.0*	B × O	10	40	12	19	81	*70.0*
O × AB	10	29	10	10	59	*43.1*	AB × O	0	0	2 †	0	2	*18.0*
A × AB	4	19	19	6	48	*52.9*	AB × A	3	15	6	3	27	*22.1*
B × AB	0	5	0	5	10	*11.3*	AB × B	1	3	1	1	6	*4.7*
Total					1038	*1038.3*	Total					435	*434.8*

* M = Malone ('49) 373 matings
R = Reepmaker ('55) 1742 matings
H = Heisto ('55) 507 matings
L = Levine — present study 501 matings
Total 3,123 matings

† Dr. Otto Hartmann, Oslo, Norway, informed the author that further analysis of Heisto's series revealed that one mother was transfused prior to the delivery of the affected infant. In the second case the husband was in A_2B so that the fetal cells, if they were in A_2, would be poorly agglutinable and theoretically could survive in the maternal circulation.

The greatest discrepancy, however, involves the matings of O × AB and AB × O, and this becomes evident from the combined series of 4 studies listed in table 4 based on a study of a total of 3123 matings selected for Rh hemolytic diseases.

Aside from Heisto's series ('55), there are 49 O × AB matings but none of the incompatible AB × O.[2] It has been suggested by Reepmaker ('55) and Nevanlinna and Vainio ('56) that all group A and group B husbands in the incompatible matings are heterozygous and therefore of genotypes *AO* and *BO* respectively. Although genetically heterozygous, group AB husbands in the mating AB × O must be considered as homozygous in terms of ABO incompatibility because all infants must be in groups A and B and are necessarily incompatible with the group O mother.

Support for this view is found in the analysis of Nevanlinna and Vainio's data ('56) on 70 cases of hemolytic disease in ABO incompatible matings which included 15 group AB husbands. These 15 matings must be AB × A or AB × B, but AB × O should have been excluded because in each of his 4 classes to be discussed below, there were affected children compatible with their mother's blood group.

The higher incidence of compatible matings among Rh negative sensitized mothers of affected infants results in a distribution of their A-B-O blood groups which is different from that of their husbands or that of a random population. This is seen in the comparison of the blood groups in the author's more recent series of 1280 Rh negative mothers which include 501 husband-wife combinations.

The higher incidence of A among the Rh negative sensitized mothers, the lower group A and higher group O among their husbands was observed in all studies in which this analysis was made. In Heisto's Norwegian population ('55) characterized by an incidence of group A of 50.6% in a random population, the incidence of group A among the Rh negative sensitized women was 55.3. The differences of groups O and A among the Norwegian sensitized women and their husbands follow the same pattern as that seen in all other studies (table 6).

In both series shown in tables 5 and 6, the greatest discrepancy is seen in the incidence of group AB which is much higher in the mothers

[2] In the authors series there were two AB × O matings but these were not included because in one the hemolytic disease preceded a remarriage with an AB husband and in the other the hemolytic disease resulted from a transfusion with a subsequently tested Rh positive donor.

TABLE 5

BLOOD GROUP DISTRIBUTION IN 1280 MOTHERS AND 501 MATINGS WITH HEMOLYTIC DISEASE

	1280 Mothers	501 Matings	
		Mothers	Fathers
	Percent		
O	41.4	41.7	57.3
A	47.0	46.1	33.5
B	7.5	7.8	8.2
AB	4.1	4.4	1.0

The 501 Rh negative mothers are included in the total of 1,280 mothers.

TABLE 6

INCIDENCE OF ABO IN NORWEGIAN POPULATION

(After Heisto, '55)

	11,644 random	745 Rh negative sensitized mothers	507 husbands of Rh sensitized women
O	37.9	30.9	46.5
A	50.6	55.3	46.2
B	7.8	8.5	5.5
AB	3.7	5.3	1.8

This series includes most of the 185 cases published by Brendemoen ('52).

than in their husbands. This is to be expected on the basis of the findings in the reciprocal matings involving an AB parent (table 4). A higher incidence of group AB mothers of Rh affected infants was previously observed by Chown ('48) and Davidsohn ('48).

As indicated above, the incidence of ABO incompatible matings in the three series of Rh hemolytic disease in which transfused mothers were excluded (Donohue *et al.*, '54; Malone, '49; Walsh and Kooptzoff, '54) did not differ much from those studies in which no mention is made of transfusion or in the author's series in which it was not possible to review the histories for this antigenic stimulus other than pregnancy. Possibly the role of previous transfusion in Rh hemolytic disease is now negligible because the current tendency is to transfuse Rh negative women or girls with Rh negative blood. However, Rh positive women or girls are as a rule transfused with Rh positive (or even Rh negative) blood irrespective of the difference in antigen c. During the period 1954 to

1956, 75 cases of hemolytic disease due to anti-c were studied in which blood groups of man and wife were available (Levine and Stroup). In 42 of these cases there was a history of previous transfusions, presumably with blood containing factor c. It is only after excluding these 42 cases that the protective effect of ABO incompatibility was noted in the 33 remaining cases and in these cases the incidence of ABO incompatible matings of 18.2 (table 7) did not differ much from the value of 19.5 in the author's series of Rh hemolytic disease shown in table 2.

TABLE 7

HEMOLYTIC DISEASE DUE TO ANTI-*c*
1954–1956

	ABO Incompatible Percent
Random matings	35
75 cases hemolytic disease	26.7
42 cases with transfusion history	33.3
33 cases no transfusion history	18.2

TABLE 8

MOTHER-CHILD COMBINATIONS

	Author	No. of Cases	ABO Incompatibility
Random, expected	Donohue, *et al.* (1954)		19.8
	Walsh and Kooptzoff (1954)		19.5
	Reepmaker (1955)		19.8
Random, observed	Wiener, *et al.* (1930)	1462	23.4
	Kirk, *et al.* (1955)	8055	18.1
	Lucia and Hunt (1950)	1167	19.8
Rh negative mothers of infants with hemolytic disease	Lucia and Hunt (1950)	120	4.4
	Donohue, *et al.* (1954)	451	7.8
	Walsh and Kooptzoff (1954)	222	11.7
	Reepmaker (1955)	1608	7.3
	Levine (this study)	293	12.6

The effect of ABO incompatibility on Rh sensitization with resulting Rh hemolytic disease is seen also in mother-child combination. In contrast to an expected incidence of about 19% and values varying from 18 to 23% in observed mother-child combinations, the corresponding values in Rh hemolytic disease are from 4 to 12%. These relationships are tabulated in table 8.

In the series with hemolytic disease there is a distinct decrease of incompatible mother-child combinations, but there was a rather wide gap of 12.6 to 4.4 in the several studies. These variations could not be explained on the basis of immunization of the Rh negative mother by random transfusions, because Walsh and Kooptzoff who excluded these cases, report a value of 11.7 while the author, who excluded only those with transfusion histories, observed a value of 12.6.

TABLE 9

NORMAL AND Rh AFFECTED INFANTS IN 70 ABO INCOMPATIBLE MATINGS

(After Nevanlinna and Vainio, '56)

	NORMAL AND AFFECTED INFANTS	
	ABO compatible with mother	ABO incompatible with mother
Normal Infants		
Preceding last normal	17	12
Last healthy child	39	11
Affected Infants		
First	15	17
Others	15	16
Total	86	56

These discrepancies could probably be resolved in complete family studies which take into account the number of pregnancies, abortions, order of birth and the blood groups of all children, healthy and affected. This was in part undertaken by Nevanlinna (Nevanlinna and Vainio, '56), who limited his study to 70 ABO incompatible matings including 142 affected infants whose ABO blood groups were determined. (In 69 dead infants and 40 additional affected infants, blood tests were not available.) The ratio of the compatible and incompatible infants in the four classes are presented in table 9.

In this series the husband is necessarily heterozygous, as already

suggested by Reepmaker ('55), so that the incidence of compatible and incompatible children to be expected is 50:50. This value is disturbed only in the first two classes but mainly in group "last healthy child," in which the ratio of compatible to incompatible affected infants was 78:22. These significant findings suggest that the essential antigenic stimulus is most frequently provided by an ABO group compatible Rh positive pregnancy resulting in a healthy infant or in an infant free from frank symptoms of hemolytic disease.

The question arises as to the source of the antigenic stimulus in the 11 ABO incompatible examples of "last healthy child" reported by Nevanlinna. Perhaps these mothers have received an intramuscular injection of blood not revealed in their histories, but it is more likely that the actual stimulus may have been provided by the "preceding" last healthy child who may have been ABO compatible with the mother. Other possible explanations will be referred to later.

TABLE 10

BLOOD GROUPS OF AFFECTED CHILDREN COMPARED WITH NORMAL

	Donohue, *et al.* ('54)		Reepmaker ('55)		Levine
	Affected Infants	Normal Infants	Affected Infants	Normal Population	Affected Infants
Group	451	1,000	1,608	68,000	293
O	51.2	46.9	50.4	45.3	49.1
A	39.2	39.9	40	42.9	39.6
B	6.7	9.7	7.5	8.6	8.2
AB	2.9	3.5	2.1	3.2	3.1

The distribution of the ABO blood groups of affected children shown in table 10 reveals a somewhat higher incidence of group O. This is to be expected if all husbands in the incompatible matings are heterozygous for A or B. The effect, however, is not striking because Nevanlinna's studies indicate that the greatest discrepancy in ABO blood group distribution is to be expected in the class "last healthy child" rather than in the affected infants. The main source of the excess of group O affected infants is derived from the high incidence of compatible $O \times O$ and $O \times AO$ matings.

The most plausible explanation for the failure of Rh positive, ABO incompatible pregnancies to provide a suitable antigenic stimulus is the intravascular destruction of the group incompatible fetal Rh positive

red cells by maternal antibodies so that they do not reach the sites of antibody production in the mother. Some support for this view is provided by the results of experiments by Stern, *et al.* ('56), who injected group compatible and group incompatible Rh positive blood into volunteer Rh negative recipients. The striking difference in the antigenic response in these two series is seen from the summary of the results in table 11.

TABLE 11

39 Rh NEGATIVE VOLUNTEERS INJECTED WITH ABO Rh POSITIVE BLOOD

(After Stern, *et al.* '56)

		Range Titer 1:	Median Titer 1:
Compatible	10/17	16-512	128-256
Incompatible	2/22	2-8	2-8

After 4 intravenous injections, 10 of the 17 compatible group produced antibodies, while only one among the incompatible group produced antibodies. The second of the latter group developed antibodies after a fifth injection.

These significant findings indicate that Rh antibodies are produced far more readily and to a higher titer following the antigenic stimulus of group compatible blood as compared with injection of group incompatible blood. Apparently, survival of the injected Rh positive red cells in the Rh negative recipient is essential for isoimmunization. As to the two of the 22 individuals who produced low-titered Rh antibodies following injection of ABO incompatible blood (table 11), one may assume that some Rh antigenicity may have resulted from slow destruction perhaps due to the combination of poor agglutinability of the red cells and low titered isoantibodies in the recipient's serum. Survival of red cells, however, is not the only explanation because in the compatible group 7 failed to produce antibodies, and among the 10 who did produce antibodies, some responded more readily than others as indicated by the first appearance of antibodies after a variable number of injections and by varying range of titers. As pointed out by Owen, *et al.* ('54) it would be interesting to determine whether or not there is a higher incidence of Rh positives among the mothers of the 7 resistant or tolerant recipients.

By analogy, one may state that in contrast to an ABO incompatible pregnancy, a compatible pregnancy provides favorable conditions for survival of the Rh positive fetal blood in the Rh negative mother. Among

the ABO compatible pregnancies, however, there are two strikingly different sorts of obstetrical histories. In one—by far the smaller group—the first Rh positive infant is normal or even mildly affected and the second and all other Rh positive infants are severely affected. In the contrasting and by far the larger (control) group, the Rh negative mother delivers two, three or more ABO group compatible Rh positive infants free from hemolytic disease. (In both classes, those giving clear-cut histories of transfusions of Rh positive blood or abortions should be excluded.) In this comparative study the mother's parity, order of birth, and birth rank of the first affected child should be recorded and compared with the control group of Rh negative women of equal parity who fail to produce antibodies. With this selected family material—limited to ABO compatible pregnancies—it should be possible to determine the role of acquired tolerance, if any, or lack of genetic capacity to produce antibodies in order to explain the absence of hemolytic disease in ABO compatible pregnancies. A high incidence of Rh positive mothers of Rh negative daughters should be associated with tolerance or little if any hemolytic disease, while the combination of Rh negative mother and daughter should yield many more examples of hemolytic disease. If, under the latter conditions, hemolytic disease does not appear, one may assume a lack of the genetic capacity to produce antibodies.

The production of Rh antibodies in the face of a group incompatible pregnancy is an unlikely event unless the infant's Rh positive red cells manage for one or another reason to survive long enough to provide an antigenic stimulus, *e. g.* a very low titer of anti-A or anti-B in the maternal serum and poor agglutinability of the fetal red cells. At this point one may also mention another set of circumstances which would permit survival of group incompatible fetal red cells of normal sensitivity. This deals with another example of possible acquired tolerance if the Rh negative women, *e. g.* those of group O with group A husbands, were daughters of group A mothers and thus acquired tolerance manifested by failure to produce anti-A when stimulated either by group A offspring or injected with group A red blood cells or A soluble substance.

The findings presented may have a bearing on the mechanism of transplacental isoimmunization. If survival of fetal red cells in the maternal circulation is a condition for isoimmunization, this would suggest that it is the intact fetal red cells which find their way into the maternal circulation either during the course of the pregnancy (Levine, '43, '44) or at the delivery (Davidsohn, '45) of the "last healthy"

ABO group compatible child. It is assumed that this passage of fetal blood into the maternal circulation occurs in all pregnancies and that the failure on the part of many Rh negative women to produce antibodies as a result of group compatible pregnancies in the absence of acquired tolerance is determined genetically.

It has been calculated by Reepmaker ('55) that in the absence of protective effects of ABO group incompatibility, there would be an increase of 23 % in the incidence of Rh hemolytic disease. Incidentally, these findings offer a basis for better prognosis in future pregnancies on the part of Rh negative nonimmunized mothers of ABO group incompatible matings. The prognosis is still better in the specific mating AB Rh positive husband × O Rh negative mother. This aspect will be discussed in future publications.

SUMMARY AND CONCLUSION

In any discussion as to the fate of gene *d* in selection and the effect of compensation, or the possible role of acquired tolerance, it is now evident that one must take into account the protective role of ABO incompatibility in reducing the incidence of Rh hemolytic disease.

ADDENDUM

In the series of Owen, *et al.* ('54) there is an indication that acquired tolerance may possibly play a role in the class listed in table 1 as "no antibodies" after three Rh positive pregnancies since the disproportion of positive and negative maternal grandmothers is considerably greater than in the series of hemolytic disease. In the 17 cases of antibodies but no hemolytic disease, however, the next pregnancy with an Rh positive fetus would certainly result in an affected infant. The findings in these two groups could be explained also if the "no antibodies" class had a high incidence of ABO incompatible matings while the "antibodies" group had a high incidence of ABO compatible matings.

The findings presented provide substantial evidence that the intact group compatible fetal red cells find their way into the maternal circulation. More direct evidence was supplied by Dr. A. Richardson-Jones (oral communication) who with the aid of a sensitive technic for the detection of a very small number of Rh positive red cells in a mass of Rh negative red cells demonstrated fetal Rh positive cells in the circulation of the Rh negative mother. This important observation was made

in Rh negative mothers tested during the last trimester of their pregnancies. Dr. Richardson-Jones estimates a ratio of 1:2000 — 1:5000 fetal red cells to maternal red cells.

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AN ANTHROPOGEOGRAPHIC EXCURSION AROUND THE WORLD[1]

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UNDER the aegides of the University Museum of the University of Pennsylvania, the Wenner-Gren Foundation for Anthropological Research, Incorporated, the Research Institute of the United States Air Force, and assisted also by *LIFE* magazine, my wife and I made a trip around the world, westward, taking 166 days. We left home on October 15, 1956, and returned on March 29, 1957, having visited en route Japan, Korea, Formosa, the Philippines, India, Nepal, Ceylon, Pakistan, Saudi Arabia, Italy, and France. In each country mentioned an effort was made to call on local anthropologists or cognate scholars, to see as much country as possible, to study skeletal and archaeological collections, and to look at people. Over 4,000 photographs were taken, about equally divided between black-and-white and color.

Moving about fairly rapidly, although comfortably, in heat and cold, and at various altitudes, and being plied with hospitality in all quarters, we saw and heard more than could be immediately digested, and it has not all been assimilated yet. This account is not a scientific document, nor even a contemporary one in its feeling and spirit; it is meant to be more like the travel notebooks produced by naturalists in the more leisurely and less sophisticated days of a century ago, when the world

[1] On April 12, 1957, as a participant in the Wenner-Gren conference on Natural Selection in Man, held at Ann Arbor under the leadership of Professor James N. Spuhler of the University of Michigan, I gave an impromptu talk on my recent trip around the world, using a set of color slides as framework. This was not a "paper" in any sense of the word, as no paper was involved in it outside the slide mounts. This written effort is a five-months late post-mortem attempt at recapitulation.

was still full of wonder, the *National Geographic* had not yet been invented, and a man could still interest himself in every living phenomenon without appearing naive or stepping on someone else's tender toes.

After landing at the Tokyo airport, our first stop was the International House of Japan, where we became the guests of Gordon and Jane Bowles. For over three weeks Gordon and I were able to renew our old association, and discuss particularly the many problems of human biology in Japan, where he was born and where he has studied and taught at various intervals over his entire life as a scholar. From him and from his Japanese associates [2] I learned as much as I could absorb in the time available. Together we went Ainu-watching on Hokkaido, and also visited the Kyoto-Nara-Tenri area; we also examined the famous Ubayama shellheaps and visited Father Marringer's mission museum. Under other guidance we visited the mountain country back of Kyoto and the fishing villages outside of Osaka.

Japan is often divided into three main geographical provinces with cultural overtones; Old Japan is the Inland Sea-Nara-Kyoto-Osaka region, comprising southern Honshu west of Lake Biwa and the two islands of Kyushu and Shikoku; New Japan is the rest of Honshu including the Tokyo-Yokohama area; the third province is Hokkaido. The " New Japan " part of Honshu can be further divided into the warm eastern coastal plain, the mountain core, and the cold, snowy west coast. Each of the three major areas, and three minor ones, has its distinct anthropogeographical problems.

During at least one of the glacial advances of the Pleistocene, the three southern islands were without reasonable doubt accessible from the mainland, to man as to other fauna. There is no reason therefore why archaeological remains comparable to those from the Choukoutien and other mainland Chinese sites should not be found, and fossil man as well. That they have not is probably due mostly to a paucity of interest. So firmly has the Japanese origin myth been imbedded in the minds of the people that to look for something older than the first man would, until the Emperor's recent voluntary demotion from godhead, have been, if not sacrilegious, at least in poor taste. In gravels in the Tokyo region, Father Marringer and the Meiji University staff have actually found flake implements typologically comparable to industries

[2] Thes included Professor Y. Iwamura, J. Kawakita, S, Kodama, T. Mabuchi, M. Oka, K. Segawa, A. Suda, S. Sukihara and H. Suzuki.

on the mainland and in southeast Asia, but their exact age is not yet known. Father Marringer's own feeling ('56: 175-193) is that they are immediately post-glacial and represent a survival in vacuo of a much earlier industry. With Gordon Bowles we visited a Mesolithic site at Asamushi, near Sendai in Northern Honshu, where we collected a few pieces of a locally well known pre-pottery industry known as Iwa Juku, after its type site near Tokyo. After Iwa Juku comes the famous ceramic Jomon culture, the first industry to yield human remains. These have now been found from all periods. I had an opportunity to examine many of them at Kyoto. Although variable, they are definitely not Ainu, in the sense of the present Ainu of Hokkaido, nor are they very Mongoloid. The Jomon people, concentrated along the coasts where they ate quantities of shellfish, resembled cranially the predominant population element of the coastal fisherman today; they were brachycephalic and more Alpine than Mongoloid-looking. The heavily Mongoloid element apparently first arrived with the invasion, from Korea, of the Iron Age rice-cultivating Yayoi people, some of whom were also long faced and convex-nosed. From time to time other Koreans have entered Japan as craftsmen and been absorbed.

If one looks at Japan in terms of the mountains-coast dichotomy, it is clear that the most Mongoloid people live in the mountains, that the fishermen of the coast are predominantly Alpine, and that the city people have developed a type of their own which is brachycephalic and long faced, with relatively little Mongoloid appearance in the anatomical structure of the malars and nose. Various explanations were given me by my learned amanuenses; that the isolation of upland villages and villages on the west coast have so fostered the growth of local populations that many new types have arisen; that there has also been a continuous selection of the sedentes-migrants character by which the narrow faced people have been drawn to the cities (Shapiro and Hulse, '39; for the I. Q. aspect of a similar situation, see Scott, '57: 311-329), and that upper class Japanese have deliberately bred a Samurai-looking type from second marriages with geishas.

TABLE 1

	SEX	AGE	STATUS
NARROW FACE	Male	Old	Higher
BROAD FACE	Female	Young	Lower

The narrow faced condition, along with light skin color, is definitely the more desired and sought after. By "seeking after" we include the use of artifice; cosmetic surgery to build up the nose and remove epicanthic folds is a thriving business in Japan; so is the manufacture of skin-bleaching substances, and of false breasts and buttocks. While at present there may be an element of imitation of the Caucasoid ideal in the motivation of these steps, the great motivation antedates our own (American) brief period of being chic, and goes back to the ancient Samurai ideal, in fact to the inspiration of the horse-faced and horse-riding invaders from whom the nobler Japanese are believed to be more largely descended than their commoner fellow-citizens. It is my own feeling that, all else equal, a gerontomorphic Japanese, to use the younger Marett's word ('36), is somehow better suited by temperament to endure the crowded life of a Japanese city than his moon-faced cousin, and that we have a principle here which can stand exploration in other countries. If I am right, then Professor Suzuki's dilemma, of how the embodiments of his mesocephalic and platyrrhine Mediaeval Japanese skulls sired the modern brachycephalic and leptorrhine urban Japanese, may be on its way to a solution.

Hokkaido is believed to be a separate anthropological province because the straits which separate it from Honshu are too deep to have been dry in glacial times, and because the Japanese still feel an even greater aversion to the idea of being descended from the hairy and dirty Ainus than they (until recently) did to finding a man older than the sun goddess's offspring. Despite a body of linguistic evidence which carries Ainu place names as far south as Lake Biwa, and the historical account of how the Japanese drove the Ainu north out of Honshu, and despite the patent antiquity of the Ainu in Hokkaido, most Japanese scholars now claim that they were recent arrivals from the north, in fact not much earlier on the spot than the Japanese themselves. One reason is the lack of Ainu skeletal material more than 300 years old. However, skeletal material is scarce in all countries where the ground is frozen many months of the year. Ainu burial customs do not promote preservation.

During the last three years archaeologists from first Meiji and then Hokkaido University have been digging sites along the northern shore of the island, and turning up amazing materials. In a number of separate sites, distinguishable in terms of soil type and depth but not by mutual stratigraphy, they have found (1) an assemblage of large

obsidian blades with carinated steep scrapers, similar to my Kara Kamar III material from northern Afghanistan, there dated at more than 34,000 years old (Coon and Ralph '55: 921-922); (2) a similar assemblage but with finer blades, and including burins; (3) an even finer assemblage of blades, and with burins and projectile-heads, the latter retouched part way across the back with what seems to have been pressure-flaking; (4) microliths; (5) a kind of arrowhead resembling the North American "woodlands," with pottery.[3]

Not only is the sequence still tentative, but the C-14 dates are not yet in. In any case, these interesting discoveries show that Hokkaido was at one time in the same general archaeological world as north central Asia, eastern Siberia, and early North America. Whether or not its evolved Stone Age cultures extended across the stormy but narrow waters of the Tsugaru Channel remains to be discovered. As not a single pre-pottery cave site has yet been dug in Japan, almost anything can turn up.

Returning to Hokkaido, we find that about 1,000 years ago a people called Moyoro invaded Hokkaido from the north, bearing ivory and bone implements with flint points set into the bone; their culture was more or less of the Bering Sea type. Being entirely coastal, they settled at Abashiri, where some of their skulls have been dug up. These are big, heavy, and Eskimoid. The Jomon people also got to Hokkaido, but in quite late Iron Age times, and some of their skulls are available for inspection in Professor Kodama's museum. These are very variable, not simply, or even predominantly, Alpine as in the earlier southern collections, but more Mongoloid and in some cases beaky-nosed.

With all this going on in Hokkaido it is not to be wondered at if the local Ainu are not all of one piece, nor should we be surprised, if we ever find Ainu remains from Honshu, if they should turn out to be different from the living and recently dead Ainu of Hokkaido. However, when one surveys Professor Kodama's vast array of a thousand Ainu skulls, several things meet the eye at once. Although big skulls, of majestic architecture, they look less like modern European skulls than the living races resemble each other. This struck me all the more forcefully because the day before seeing them I had stood next to an Ainu of my own age and except for his greater interorbital distance and lower nasal bridge, we might have been brothers.

[3] In his 1956 excavations Professor Kodama was accompanied by an American Fulbright botanist, Mr. Theodore Bank.

They are more massive than most European skulls; the canine fossa is lacking, and the teeth are larger. Despite the wholly Caucasoid orbit, there is a faint Mongoloid look that defies pinpointing, except in the fact that many of the Ainu teeth are shovelled, without, however, being procumbent as in many Japanese skulls. Furthermore, according to Professor Kodama, the Ainu teeth have an incidence of 30% of enamel pearls, a condition rare in other populations, except for the Eskimos, and one indicating a considerable genetic isolation.

It is Professor Kodama's stated opinion that the Ainu skull falls closest to the pre-Neanderthal specimens from Europe, such as Krapina, rather than resembling the Upper Paleolithic Cro-Magnons, and that the Ainu are thus an exceedingly ancient and primitive Caucasoid race; this is borne out, he says, by the neuroanatomy of the Ainu motor area, which is comparatively simple. While Ainu brains are larger than those of the Japanese, he said, they are not as complexly organized. Professor Kodama made his vast reputation not by collecting skulls or digging up flints, but in neuroanatomy. I have a lively respect for both his erudition and his wisdom. The problem of Ainu origins has not yet been solved, but the solution is on its way.

From Japan we went to Korea as guests of the United States Air Force and of the McGraw Hydrocarbon Company at Chungjo. With a recently returned Harvard graduate student, Mr. Kim Jong Hak, we explored a cave at Puk-Ha-Ri, just north of Tanyung. As no prehistoric archaeology had been done at all in Korea, except for some shell-mound work on offshore islands, it seemed a good idea. Caves are rare in Korea; the limestone is extremely dense and hard, and has few solution cavities. This cave is ideally situated above a river, and indeed, has a spring inside on one side; the walls slope outward and downward, and the fill is soft yellow earth. With local help we went down 80 cm through sterile earth to what seemed to be Neolithic material, including one typical celt-sharpening stone. I was and still am haunted by the idea that Sinanthropous remains must be just as abundant in Korea, where we can go, as in China, where we cannot. Future work will, I hope, tell whether Puk-Ha-Ri is the right site or not.

Compared to Japan, the racial situation in Korea seems fairly simple. A stature-weight cline undoubtedly exists from north to south, following Bergmann's rule. Head and face form are relatively uniform, with extreme brachycephaly combined with long faces and narrow noses; at least part of the Japanese ideal seems to have its prototype here. My

feeling was that the Koreans are a kind of Turk; I was reminded of the Turkomans of the Gurgan Plain in Iran not only by their faces but also by the common occurrence of lean body build, and the occasional green eye and blond mustache hair.

In Seoul we were most graciously received by President Yun Il Sun of Seoul National University; he introduced us to Dr. Rha Sea-in, head of the Anatomy Department, and Dr. Han Pumsuck, the director of the Public Health School. With these two medical men I went into the

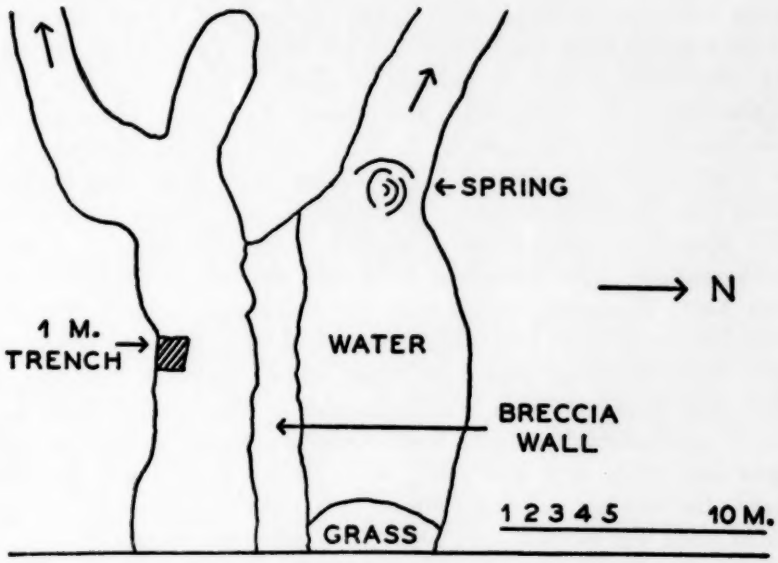

FIG. 1. THE CAVE OF PUK-HA-RI, KOREA.

question of the anatomy of the Mongoloid face; it is very simple, they said, and showed me that the key to the whole complex is the position of the temporal muscles, which are attached farther forward on the frontal bones than they are in Caucasoid skulls. In the area behind the orbit they press farther forward than they do in the Caucasoid skull, and reduce the depth of the orbit, pushing the eyeball forward in its socket. The Mongoloid masseters are also attached farther forward than in the Caucasoid skull. The whole Mongoloid mandibular musculature is hung relatively far to the front. The nasal skeleton also differs in several ways, being more built-in than the Caucasoid apparatus and forcing the eyeballs farther apart. Later on I learned from a noted

eye-surgeon in Shillong, India, Dr. B. G. Guha (the anthropologist's brother), who operated daily on both Caucasoid and Mongoloid eyes (Khasis, Bengalis, and Europeans), that of the two the Mongoloid eyeball is the smaller. After seeing a number of Korean-American hybrids, who could pass for Americans, I came to suspect that the genetic basis for North European-Mongoloid differentiation, at least as far as the facial structure is concerned, is small and simply organized.

After returning to Japan we flew to Formosa, where we were warmly greeted by Professor Li Chi, director of the Academia Sinica and head of the Anthropology Department at the University of Taipei. He showed us his material from the Bronze Age site of An Yang, which, owing to the vicissitudes of war, he has had to move 14 times. He also let me see the famous An Yang skulls, and measure 8 of them. These had once been measured by Professor T. L. Woo, whose present whereabouts, if he is still alive, are unknown. These skulls, which came from sacrificial burial pits, seemed to be mostly or entirely female. Three distinct types were present; a dolichocephalic, modern North Chinese type; a heavy, brachycephalic, very Mongoloid form, and two skulls that could have been North Europeans, except that they had shovel incisors. The principal features of these two that distinguished them from the others were deep orbits and large prominent, nasal bones. However, that does not mean that their soft parts were Caucasoid, or that similar skulls could not be found among the living North Chinese population. This extremely significant series may well show, when finally studied and published, that at the very beginning of Chinese history the population of the North China plain was variable, and probably of multiple origin.

Going south to Taichung with our Assistant Air Attaché and host, Capt. Arthur Prager, we stayed with old State Department friends, Robert and Carol Lindquist, then attending the State Department Foreign language school. With them and others we made daily excursions into the mountains to see and photograph the aborigines, concentrating on the Atayals, a nation of 38,000 people who occupy a fifth of the island, less than half of which is inhabited by ten million Chinese. Head hunting helped keep the invaders at bay for centuries; now they are kept out by government decree and the fact that the aboriginal territory is too steep for rice terracing except at enormous effort. As in Japan and elsewhere, rice, both master and slave of man, feeds tens of millions while crowding them into limited areas.

The Atayals are physically variable. Some of the older women could

be taken easily for Ainus; the tattooed whisker, reaching from lip to ear, heightened the natural resemblance. Two women whom we saw could easily have been Italian; a third Maya Indian. Heavy browridges and deep-set eyes characterize many of the men. Traces of blondism of hair and eye, with fair skins, are common. In contrast to the Atayals, the other two tribes whose members we saw, the Thaos and Bununs, are brown-skinned Alpo-Mongoloid people closely resembling the pagan tribes of Luzon to which they are culturally related. The racial history of Formosa promises to be no simple web to unravel.

Another hop took us to the Philippines, for a mere 4 days; one was spent visiting the Negritos at Clark Field with Dr. William T. Ward of the Air Force research staff, and the Crow Valley tribe with Captain J. A. Simon, who took us there in a Cub airplane. Although uniform in stature, the Negritos vary enormously in other respects; one old lady could have been a Bushman, and one man looked exactly like a miniature replica of a huge Australian aborigine named Tuki whom I measured in Melville Island in 1954. Hybrids were all above the standard 150 cm level.

Next we visited Manila, where the dean of Philippine anthropology, Professor Otley Beyer, very graciously gave us two full days of lecturing, demonstration, and wisdom. In his mature opinion, no cultural change took place in early post-Pleistocene times to warrant the idea that Negritos invaded the island with a Mesolithic culture; as other pygmy fauna have been found there, he suggests that the Negritos are the descendants of earlier, full-sized inhabitants, reduced by some selectively favorable genetic agency. Quite independently he worked out the same hypothesis arrived at by Hiernaux, Adé, Gusinde, and others for the African pygmy, and by Tobias for the Bushman. It is by far the simplest and most plausible hypothesis available. He also told us and showed us many other things, which greatly enhanced my education on the subject of these islands and their inhabitants.

A son, daughter-in-law, and 4 grandchildren awaited us in New Delhi. Eighty-five of our 166 days were spent in India, 8 in Nepal, and 6 in Ceylon. These 99 days were among the most profitable of my life. We first went to Jaipur and out onto the Thar Desert, to see how deserts in India compare to others elsewhere; then to Ranchi, where we stayed with my old friend and former teacher, Professor B. S. Guha, once head of the Department of Anthropology of the Government of India, and now director of the Bihar State Tribal Institute at Ranchi.

He took us about among the Chota Nagpur Hills, introducing us to many kinds of aboriginal people, the Oraons, Ho, Santal, Munda, Asuras, and Birhors. With us he went to Gauhati in Assam, and up into the Khasi Hills, to Shillong and Cherrapunji. Although unable to accompany us further he directed us from his driver's seat at Ranchi. In and about Cochin we saw the dwarfed Kadars of the forests, White Jews, and Malayalams; also Lake Periyar and the game reserve, Tamil country. We went with an Indian Buddhist mountaineer, R. N. Rahul, to Darjeeling and Kalimpong, and called on the Tibetan scholar, Georges de Roerich; then with Prince Peter of Greece to the Bhutanese lamasery of Pedong, and the Pedong fair; then to Kathmandu, where with John Pelzel of Harvard we joined Colin Rosser of the London School of Economics in a visit to his study-spot, the small town of Sankhu, an unspoiled gem. We also visited the great linguist, Colonel T. W. Clark, at Kathmandu. Later we went to Ceylon where we were shown a collection of new skulls and archaeological materials by the naturalist Paul Deraniyagala, director of the National Museum, and were given an entree to visit the Veddas by their special caretaker, Dr. Richard Spittle. Only three days were left for parts of Pakistan, which we had seen before.

India—here I use the word geographically only, for it cannot be divided by anyone but politicians—is a world in miniature. It has every known climate except tundra, and every known major race of mankind except the Bushman. Its people live in every known level of social complexity, from that of the simplest bands of root-diggers to that of the world's greatest statistician—Mahalanobis,—and of philosophers of the stature of Rabindranath Tagore. In one place or another and in one way or another, India has nearly everything. After 52 years of hearing and reading about India I should have known this, but it took a personal visit to have the impact hit me between the eyes. Either India is the home of all peoples, or the place where they all overlap, or, more likely, a combination of both.

Of the many tribes of simple food gatherers, I saw but three; the Birhors, Kadars, and Veddas. The Birhors, who live by catching monkeys in nets, digging roots, and trading rope for manufactured products, are small but not dwarfed people of an essentially Caucasoid body habitus and facial configuration. They must be among the oldest inhabitants of India, pre-Munda and pre-Dravidian, although they speak a form of Munda. The Kadars, who are root-diggers and honey-collectors, live the simplest possible kind of life. Before obtaining iron tools in trade

they used only a digging stick, tipped with a roughly flaked stone. Some of the Kadars whom we saw in a single community were essentially Negritos; others looked Veddoid, or Australoid, or in between. The Veddas, who hunt with the bow (the Birhors and Kadars do not usually use it) are like the Birhors, miniature Caucasoids of a very basic and variable kind.

After I had seen these three tribes it came to me why the Dravidians and Aryans had been able to adapt themselves to the miserable heat of the Indian plains; they absorbed, seriatim, remnants of these earlier peoples of the same general strain as themselves, peoples whose adaptation to the terrain went back to the Pleistocene. Thus they survived, as the Anglo-Indians have in turn, while the full-blooded British have departed. The capacity for survival is not only a matter of climatic protection, but of neurological adaptation as well, which is a broad term embracing cultural phenomena.

Then it occurred to me why the Mongoloids had been able to live in the heat of Indo-China, Burma, and Siam—because they had been preceded in the steaming forests by earlier Mongoloids, the People of the Yellow Leaves, who had been able to transfer their genetic basis for survival without a loss of essential Mongoloidism. Many Mongoloids have come into India at one time or another, with different results.

In Calcutta I was privileged to examine certain still unpublished skulls from the Indus Valley civilization and this was as massive a milestone as the examination of the An Yang skulls in Taipei. These were equally variable, including some oversized Caucasoids that might have come from Sumeria or Denmark, some gracile Mediterranean crania, one patent Australoid, and one full Mongoloid, as out of place in the Indus valley in the third millenium B. C. as he would be today. Another principle was indicated, that multiplicity of genetic origin is an ancient thing in civilized places, while the mowing hand of natural selection cuts the originally variable grain to standard sizes. There were no autochthonous Mongoloids in India to do the job of the ancestors of the Birhors, Kadars, and Veddas.

When we moved into the Chota Nagpur hills, three kinds of people were in evidence: (1) The Caucasoid Birhors, who spoke a language probably not their own; (2) the Australoid Oraons, speaking Dravidian; (3) the phenotypically heterogenous Munda-speaking peoples, including the Munda proper, Ho, Santal, and Asuras. Their languages are related to Mon, Khmer, and other forms of speech native to southeast Asia,

whence their early food plants and shifting agriculture seem to have come. In a nutshell, the men are almost but not entirely Australoid, and the women are, more frequently than the men, partly Mongoloid. The Asuras, hereditary blacksmiths and smelters, are somewhat Negroid as well, and Tasmanoid or Negroid individuals can be found marginally among the Munda. What we have here is a blend of at least three stocks—Negrito, Australoid, and Mongoloid, in varying proportions, with the Mongoloid partially linked to the female sex.

Moving up to the Khasi Hills we found a light-skinned and essentially Mongoloid people living above the mosquito belt of 4,000 feet. Linguistically and culturally they are tied to Burma and Indo-China, if not indeed to Polynesia. Their plateau is wet as well as chilly; it has the world's heaviest rainfall. Over the edges of the plateau, down the slope, other peoples are settled like layers in a cake; in the next set of hills, at 2,000 feet or so, live the Garos, much darker-skinned than the Khasis, and less frequently Mongoloid. Later, in Ceylon, we found the same thing. The Singhalese living on the steamy plain are long and lean in habitus, long headed, narrow faced; as one moves upward through Kandy to Nuwara Eliya, at 6,000 feet, they become shorter, stockier, and lighter skinned; the frequency of epicanthus also increases with altitude.[4] Here we have in two separate parts of the subcontinental area an identical cline linking Mongoloid racial characteristics with altitude, similar to that known to exist in Madagascar (for a theoretical study of racial clines, see Womble, '51: 315-322).

However, the world's sharpest racial frontier is probably the vast lip of the Himalayas along the whole southern border of Tibet and southwestern China, from Kashmir to Burma. All along the arc, above 14,000 feet, are Tibetans, fully Mongoloid, whether called Bhotias, Sherpas, or whatever. Below them come a host of tribes: Dotiyals, Magars, Gurungs, Tamangs, Rais, and Limbus in Nepal; Lepchas in Sikkim, unclassified in Bhutan; and over in the Northeast Frontier Area Mikirs, Miris, Abors, and Mishmis, and finally Nagas. These peoples are variously Mongoloid depending on altitude. Many of them, like the Lepchas and Limbus, actually look quite European in an Alpine sense, and in fact resemble the Caucasoid element in the Indonesian complex, particularly, in terms of the present report, the Formosan Atayals.

[4] This will be shown in an extensive series of Singhalese measured by the late Dr. J. R. de la H. Marett, now being written up by Howard Stoudt of the Harvard School of Public Health.

That malaria may play a selective role in keeping the Mongoloids above 4,000 feet is no new idea to the Mongoloids themselves. They fear the disease and most of them know better than to try to live at a low altitude. However, something else must operate to keep the Caucasoids below 14,000 feet. That factor may well be a lack of high altitude adaptation concerned with libido and the oxygen transfer from mother to foetus; this is known by analogy from studies in Peru and Bolivia. Even among the altitude-adapted Tibetans, libido increases markedly on visits to an altitude of 4,000-7,000 feet. My authority for this is a man in a good position to know; the former police-chief of Kalimpong.

At the foot of the Himalayan slope stretches a vast forest, the Terai, filled with savage beasts. Although now nearly uninhabited, it was occupied within a century ago by a wild, jungly people with black skins and thick lips, who hunted in its shaded aisles with bows and arrows. Today some of the Munda-speaking peoples of Central India have moved up to its borders to work on tea plantations and the railroad.

Among the Aryans themselves, a distinction may be made between those who live on hilly country and those who cling to the flat Indo-Gangetic plain, like fish in an aquatic environment. Col. Clark suggested that the hill-people may represent an invasion of shepherds travelling on foot or horse, and the plainsmen one of cattle people riding in ox-carts; he is working on a linguistic basis for this distinction. Guha, too, pointed out that the distribution of Aryans in Assam coincides precisely with the altitude map, covering the flatland where bullock carts can go without road-building, and the moment one leaves the plain, he finds himself among more or less Mongoloid people speaking non-Aryan languages. In Nepal the Khass, the warrior caste of Aryans stretching from one side of the country to the other at about the elevation of Kathmandu, presumably represent the nonvehicular wing of the Aryan migration. The Newaris, the highly civilized Tibeto-Burman speaking occupants of the Kathmandu valley, who are part Hindu and part Buddhist, look for all the world like Chinese.

In Cochin we saw that cities as well as mountains can serve as refuge areas. There we walked down the famous street of the White Jews, who have lived there for nearly two millenia, keeping themselves out of the sun's direct rays under roofs and lattices, still as white as their ancestors in Palestine could have been; however, only 150 out of a former 1,500 are left. Thus through a choice of occupation and man-

made environmental protection, bolstered with a breeding pattern of their own choosing and enforced by religious sanctions, men can produce their own isolates. Culture, in other words, is as much a part of our total environment as solar radiation and altitude, and culture itself may be a product of man's physical differentiation. The thing is circular.

After India even Paris is a letdown. On the rest of our trip we measured 7 Mahri-Socotran-speaking Arabs at Dammam, where Dr. Charles Matthews of Aramco was linguistically debriefing them. Thus I was able after over 20 years to make a correction for Bertram Thomas's erroneous head lengths in his still unique anthropometric series of these people (Thomas '32: Appendix I; Coon '39: 427-428). They are not, as his measurements implied, and pictures belied, microcephals.

In Rome we stayed with the hospitable Baron and Baroness Alberto C. Blanc, and saw his hand-axe site at Torre in Pietra; in Florence we stayed with Professor Lidio Cipriani, from whom I obtained a selection of 1,000 photographs of racial types for my projected *Races of the World*. I did a little business at the Musée de l'Homme in Paris and then reached home bewildered and exhausted. Only now are sights I saw and words I heard beginning to sort themselves out at all clearly, permitting me to write a report as old-fashioned and frankly preliminary as this one.

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THE STUDY OF NATURAL SELECTION IN PRIMITIVE AND CIVILIZED HUMAN POPULATIONS

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THE principle of natural selection as a guiding factor in human evolution is today universally accepted. However, although in recent years the mathematical papers of Fisher, Wright, Haldane, and others have greatly advanced our understanding of the manner in which the changes in gene frequency which constitute biological evolution come about, our knowledge of the actual workings of natural selection in human populations is almost nil, but little advanced today beyond that expressed by Wallace in 1871 in his well-known paper on "The action of natural selection on man." There are currently evidences, as in a number of recent essays, of a growing effort to extend our insight into many aspects of the problem (e. g., Chance and Mead, '53; Etkin, '54; Coon, '50, 55; Dobzhansky and Allen, '56). In a way, these essays as a group only point up the gap between the apparent response to selection which has characterized human evolution and our lack of detailed information with regard to the relation between natural selection and specific human characteristics. Field studies which have included as a stated objective the analysis of selective pressures in human populations, such as those of Birdsell ('50, '53) and Kluckhohn and Spuhler (Kluckhohn and Griffith, '50; Spuhler, '50), can almost be counted on the fingers of one hand. Contemporary man cannot be understood without a vast array of such information. Furthermore, at this moment one of the most actively discussed topics in human biology is the genetic risk of the increased amounts of ionizing radiation to which human populations all over the world are being subjected. A critical factor in these discussions is the

nature of the assumptions made concerning the amount and manner of action of the selection to which today's man is subject.

When one contrasts the harshness of life for the African Bushman or the American Eskimo with conditions in the United States today, it would at first glance seem almost self-evident that we who enjoy the latter are functioning in a cotton-batting existence where each zygote, whatever its frailties, is—subject to a few accidents and socio-economic happenstances—virtually assured of a long, sheltered, and—more important from the genetic standpoint—almost equally reproductive life. This self-evident proposition has been repeated in recent years with an almost hypnotic regularity, with relatively few raising a doubting hand. Notable among these latter is S. J. Holmes, who wrote: "To talk . . . of natural selection as if it were practically done away with among civilized human beings, as many writers have done, is eminently absurd. In fact, it may be doubted if civilization has effected much diminution in the intensity with which natural selection acts on the human species. While much progress has been made in the art of saving life, there are many new forms of selective elimination which have been brought into play as a result of our civilization, and especially of our industrial development" ('24: 355).

Those who urge that the selective pressures on human populations are rapidly diminishing often cite the decrease in infant mortality and the preservation of persons with genetically determined diseases as proof of this thesis. It is true that infant mortality, rather than being the 500 per 1,000 of some primitive tribes, is now approximately 30 per 1,000 in the United States. This undoubtedly has significance from the standpoint of natural selection. But yet we are in no position to reach a judgment as to how much infant mortality is meaningful in the selective sense and how much is fortuitous, in the sense that any infant, regardless of genotype, who happens to be in a particular place at a particular time is destined to die. It is also true that modern medical practice is preserving the lives of many children and adults with genetically conditioned disease who a few centuries ago would have died within a short time after the appearance of their disease. And yet, to consider only a single example, juvenile diabetes, while undoubtedly a certain number of these children live and reproduce who would not have done so before the introduction of insulin therapy, reproductive expectancy as a whole is still greatly reduced. While the general principle that there has been some relaxation in certain types of natural selection seems

sound, it is important to recognize that the genetic consequences of the apparent relaxation in these types of natural selection are not clear, nor is it any clearer where these apparent types of selection fit into the total picture of selection on human populations.

The general thesis which I would like to present is the following: The need is great for a variety of parallel studies on selective factors in advanced and primitive societies. Such studies are at the same level of importance as investigations on spontaneous mutation rates, the nature of the gene, skeletal remains, or the effects of irradiation on human populations, in our efforts to understand man's past and to predict his future. These studies, especially as they pertain to primitive groups, present real practical and methodological problems, and for these reasons, as well as a relative lack of interest, progress in this area has lagged far behind that in the other areas just mentioned. Yet by careful selection of projects, important advances can be made in the relatively near future. Finally, there is a certain urgency to the problem, so rapidly are primitive societies being disrupted.

This thesis is for the most part so broadly worded that it would appear to be the genetic equivalent of a political platform which is against sin and for mother love. However, there is one specific point on which considerable disagreement might arise, and this is with regard to the present feasibility of significant studies on natural selection. It is to this general question that the remainder of this presentation will be devoted. More specifically, three different areas will be examined in which the time would seem to be at hand for some rather significant observations. Dr. Levine has discussed still a fourth area in this same symposium. It should perhaps be emphasized that these areas are arbitrarily selected as examples, although, as will become apparent, there is a certain design in the choice of these examples.

The Variability in Individual Reproductive Performance in Primitive and Civilized Cultures

In the strictly biological sense, the genetic worth of a newly formed zygote is measured in terms of the number of descendants which will survive it. In the broadest sense, selection is operative when in a population the average reproductive performance departs from simple replacement values and/or individual members of the population contribute disproportionately to the next generation. It is this latter aspect of selection, between individuals of the same species, which has attracted the

most attention and is usually thought of when the word "selection" is used. This selection may be either on biological or cultural grounds. It will often be difficult to distinguish between the two types. The focal point of this essay is to define representative areas in which the *changes* in selective pressures inherent in the transition from a relatively primitive to a relatively advanced culture can be isolated and characterized. Studies of the manner in which communities and the individuals of whom they are composed replace themselves offer unusual opportunities from the comparative standpoint. The differences in individual fertilities in contemporary Western civilization and their possible genetic implications have been the subject of repeated comments. No one seems to have improved materially on Pearson's statement of 60 years ago: "It is a point which seems to me of the utmost significance that, allowing for the proportion of unmarried in the population, about ⅕ to ⅙ only of the adults produce quite one-half of the next generation, and any correlation between inheritable (physical or social) characteristics and fertility must thus sensibly influence that next generation" (1897: 83). Very much less has been written concerning fertility differences in primitive societies. Reliable data on this subject are scarce, since the early explorers and even anthropologists were little concerned with studying the fertility of the natives, and by the time the interest of the problem was recognized, the primitive state was seriously disturbed. Much of what is available has been compiled by Krzywicki ('34). As he points out, it is unsatisfactory other than as a very rough guide. Thus far, despite a considerable search of the literature, no single description of the distribution of individual completed fertilities in a truly primitive "hunting and gathering" society has come to light.

However, in recent years, extensive and fairly reliable data have become available for a number of relatively unsophisticated areas. These are all beyond the hunting and gathering stage and well into the agrarian epoch. By way of examples, table 1 gives some recent data from Africa and Pakistan. The sociological factors which may have altered the findings from the situation which existed several hundred years ago are discussed in detail in the original presentations. In addition, the figures are subject to a number of errors, also discussed in detail in the original presentations. Furthermore, to be entered into the table, a woman must have survived the childbearing period. The three sets of data are not strictly comparable, but agree on the important point of the wide distribution of individual fertilities.

TABLE 1

Number of children ever born to women aged 45 years and over, in four different areas

Number of children ever born	Agogo Township, Ashanti Territory The Gold Coast *	Two villages East Pakistan †	Liberia ‡	New South Wales, Australia §	U. S. A.**
0	11	2	7	1,110	2,622,060
1	8	2	4	583	1,459,460
2	19	3	7	581	1,676,700
3	14	6	1	644	1,318,940
4	29	3	4	702	962,780
5	26	9	6	813	1,179,400
6	34	10	5	855	
7	39	15	8	976	
8	31	5	7	963	787,200
9	26	8	1	847	
10	32	5	3	786	
11	16	5	1	568	
12	6	4	1	422	
13	2	1	2	226	
14	1	1	1	129	
15	1	0	1	57	
16	0	0	0	39	
17	1	1	0	12	331,220
18	0	0	0	5	
19	0	0	0	2	
20	0	0	0	2	
21	0	0	0	1	
22	0	0	0	1	
23	0	0	0	0	
24	0	0	0	1	
30	0	0	0	1	
Total	296	80	59	10,276	10,337,760

* Collected during one fortnightly (field study), 1945. v. Fortes 1954.

† Collected over several months (field study), 1953. v. Aird 1956.

‡ Collected over several months, 1956. I am most grateful to Drs. A. H. Jonkers and Frank Livingstone for permission to use these unpublished data, based on the reports of post-menopausal women living in the native villages of the Firestone Plantation.

§ Collected in 1898-1902, Powys, 1905. Unlike the other three studies, this concerns women aged 46 and over.

** U. S. Decennial Census, 1940. Government Printing Office. The entry "single women" in the census data has been equated to childless.

There is evidence from many parts of Africa that at present infertility is more common than was the case 20 or 30 years ago. This is often attributed to the spread of venereal disease, but of course the introduction of venereal disease to Africa goes back much further than that. It is not at all clear to what extent the figures given in table 1 depart, for this and other reasons, from those which might have been observed several hundred years ago. Data from other comparable areas in Africa show about the same amount of infertility (*e. g.*, Mitchell, '53), and it may be that even under circumstances most favorable to reproduction, a minimum of 3 to 5% of women will remain childless. Under unfavorable primitive conditions, the sterility rate may be appreciably higher. Thus, Malaurie, Tabah, and Sutter ('52) record that among 51 postmenopausal Greenland Eskimos, 8 were sterile.

How do these figures compare with those for contemporary cultures? Fisher ('30)—and before him, Pearson—has argued that the most important cause of genetic change in Western civilization is differential fertility. In his argument, Fisher drew heavly on the data of Powys ('05) on the number of children ever born to 10,276 married women dying age 46 or over in New South Wales from 1898-1902. These data are also reproduced in table 1. There is room for debate as to how typical data from Australia at the turn of the century are for Western civilization in general, but unfortunately, such is the paucity of good data on this problem, these were apparently the best Fisher could find. In these data, the most fertile 50% of the women gave birth to 76.4% of the children. By comparison, in Agogo 50% of the women were responsible for 69.7% of children ever born, while for Pakistan and Liberia the corresponding figures are 69% and 78.5% respectively. It would appear from these data that differences in individual fertilities, of a magnitude which led Fisher to consider differential fertility as the most important agent of genetic change in contemporary society, probably extend far back in the history of man.

Data on familial correlations in fertility are as inadequate as data on the distribution of individual fertilities. Fisher ('30) in an analysis of Pearson's (1899) data concerning the numbers of children born to mothers and daughters in a thousand cases extracted from the British peerage, finds a correlation of 0.2096 for the number of children born to mothers and daughters, and a correlation of 0.1123 for the same relationship with respect to granddaughters and their paternal grandmothers, and develops reasons for regarding this in some indeterminate amount as

genetically determined.[1] He then writes: "We have seen that by no means extreme genotypes have rates of reproduction in a ratio higher than 2 to 1, and if for simplicity we imagine a population consisting of two strains, which, having equal mortality, differ only to this extent in fertility, it is easy to see that the numbers of one type relative to that of the other will, in ten generations, be increased over a thousandfold. To put the matter in another light, if at the beginning of the period the population consisted of 97% of the less fertile and 3% of the more fertile strain, in 5 generations the 2 strains are brought to an equality, and in 5 more their situations are reversed, so that the less fertile strain is represented by 3% and the more fertile by 97% of the population. Civilized man, in fact, judging by the fertility statistics of our own time, is apparently subjected to a selective process of an intensity approaching a hundredfold the intensities we can expect to find among wild animals, with the possible exception of groups which have suffered a recent and profound change in their environment. We may therefore anticipate that a correspondingly rapid evolution has taken place within historical times in the appropriate mental attributes" ('30: 199).

The developments as regards differences in individual fertilities since Fisher wrote these lines would apparently only serve to reinforce his argument. Thus, table 1 gives data concerning the number of children in completed families in the U. S. in 1940, as revealed by the census carried out that year; the condensed form in which the data are presented hinders certain exact calculations, but by the time of the 1940 census, 50% of the women had become responsible for approximately 88% of the children born each generation.

In our present monogamous and relatively long-lived society, specifying the reproductive performance of the female of the species tends to describe the distribution of male fertilities as well. But in societies where there is polygamy and marked social pressure favoring marriage, this would not be the case. In a stimulating essay entitled "Does the fittest necessarily survive?" Shubik ('54) works out the elementary mathematics of survival in a society where the "strong" regard each other

[1] Correlations regarding fertility must be regarded in a different light than, for example, correlations regarding stature in successive generations. For example, a short person who fails to reproduce will be dropped from further consideration regarding correlation in stature between various generations, but may appear in certain fertility statistics, depending on how one elects to treat the data. This introduces complications into how one views and contrasts fertility correlations with other biological correlations.

as a threat and so are thrown into conflict, while the "weak" are ignored as presenting no challenge. But to the extent that in a society with very high marriage rates the weak later inherit, if not the earth, at least some of the widows of the strong, not only do the fittest not necessarily survive, but the reproductive differential would be even more in favor of the weak than the mere facts of life expectancy would suggest.

Two obvious conclusions emerge from these figures and considerations: (1) Striking differences in individual fertilities are not new but, with all their important genetic consequences, probably extend far back into the history of the human race. (2) These differences, considered in terms of individuals reaching reproductive maturity, are probably more pronounced today than ever before, although, in terms of reproductive expectation *at birth*, the change may actually be in the opposite direction. These are facts with which we would all agree. There can be no doubt of the evolutionary implications of these differences. Their implications from the standpoint of natural selection depend on the degree to which they are genetically determined. If there were no genetic component in fertility differences, then, while they might be a mechanism for human evolution, it would be independent of biological selection. From our present knowledge of inherited defects which directly or indirectly interfere with human reproduction, there can be no doubt that fertility is to some extent genetically determined, and that natural selection is therefore to some extent involved in these fertility differentials. Specification of the magnitude of this component depends not on further studies of the British peerage or German nobility (cf. Editorial Note, 1935), but on detailed studies of relatively stable populations not subjected to rapidly evolving socioeconomic circumstances.

At the one extreme it can be argued that if the degree of differential fertility which has obtained over past centuries has facilitated man's evolution, then the present increase will aid the adjustment of the human species to rapidly changing conditions. At the other extreme it may be argued, as Fisher ('30) so compellingly has (see also Pearson, 1897), that our present civilization replaces an earlier, eugenic set of fertility determinants with an essentially dysgenic set. The truth may not be found in either extreme. More specifically, it seems likely that some of the presumably eugenic facets of differences in individual fertilities as seen in primitive societies are still with us, but that the dysgenic facets are now more numerous than they were previously. Whether the net balance is still eugenic, in permitting appropriate genetic re-

sponses to a rapidly changing environment, even if more slowly, is a question of the utmost consequence. But whatever one's interpretation of the cause or the precise genetic consequences of the differentials, it is clear that because of these differentials the potentiality of change in the composition of the gene pool, which *is* biological evolution, is today enormous. It follows that knowledge of fertility determinants is of prime importance.

Much has been written concerning cultural determinants of fertility, as reflected in differences in mean reproductive performance between various socioeconomic groups. But within any group, there are still great ranges in fertility. To what extent these individual differences are cultural, and to what extent biological, is difficult to say. For instance, is the overwhelmed couple of today which limits its family to one child because it cannot plan for more, the modern counterpart of the Australian aborigine and his mate who killed all their children but one because they interfered with their mobility?

A comprehensive understanding of the occurrence and the cause of individual fertility differences in various societies is certainly one of the outstanding genetic objectives of our day. The timeliness of data on the very primitive societies needs no emphasis. That each society will have to be evaluated as a separate problem is obvious. Consider, for example, the matter of differences in marriage rates between societies. In the 1940 census data some 11.5% of the women were unmarried, which, in our culture, generally excludes reproduction. On the other hand, in the Ashanti village which formed the basis of the calculations given earlier, very few individuals other than the grossly defective remain unmarried or widowed (Fortes, '54), a situation characteristic of all Africa (cf. Martin, '53; Roberts, '56). In the Pakistan village studied by Aird ('57), the marriage rate was 100%; such high rates were apparently typical of almost all primitive societies (Krzywicki, '34). Now, it is common to think of a high rate of celibacy as dysgenic. In the case of women in the United States, there is an inverse correlation between years of education and marriage rate. To the extent that the more educated women tend to be a more intelligent group, their failure to marry means the loss of desirable genes from the gene pool. However, a marriage rate of 100% also has certain dysgenic implications. Two illustrations will suffice. In multiple neurofibromatosis, the fertility of affected individuals in the state of Michigan at the present time is 0.527 that of their normal siblings, with females manifesting a higher

fertility than males (Crowe, Schull and Neel, '56). However, only 32% of affected males marry, in contrast to 58% of affected females. As shown in table 2, the fertility of married affected individuals is

TABLE 2

Fertility in neurofibromatosis, after Crowe, Schull and Neel, 1956 *

Fertility all patients with neurofibromatosis	0.527
Fertility male patients with neurofibromatosis	0.413
Fertility female patients with neurofibromatosis	0.748
Fertility all married patients with neurofibromatosis	0.795
Fertility male married patients with neurofibromatosis	0.620
Fertility female married patients with neurofibromatosis	0.887

* Fertilities are expressed in the fraction of the fertility of unaffected siblings.

0.795, with females again more fertile than males. A proportion of those who fail to marry are so severely handicapped by their disease that it is doubtful whether they would marry in any society. However, another proportion fails to marry, not for reasons of physical disability but because of the disfiguring effects of the disease or its effects on intelligence. It seems likely that in a more primitive society these latter individuals would marry and propagate their defect. As a second illustration of the dysgenic implications of a marriage rate of near 100%, we might consider the relation between I. Q. and fertility. Penrose ('50) has argued that since both the very intelligent and the very unintelligent show relatively decreased rates of reproduction, there may exist a balanced polymorphism with respect to the genetic determinants of intelligence. But if, as seems possible, the intelligence requirements for marriage are being pushed upwards, then the net effect of this trend would be to shift the fulcrum of this balance toward the upper end of the scale. Whether this would offset the effects of the lower marriage rates of the more educated is debatable. Thus, in considering the genetic implications of failure to marry, it seems likely that each society will require a separate balance sheet.

As important as the causes of differences in individual fertilities, is the problem of differences in the survival rates of the children of various families, especially in primitive cultures. A related problem is the degree to which pregnancy wastage and infant and childhood mortality is disproportionately greater in large than in small families.

Krzywicki emphasizes the fact that infanticide has apparently been widely practiced by primitive societies as a means of reconciling population with available resources. If in primitive societies there were strong social pressures for modest-sized families, say two or three, then here is a factor to offset differential fertility; a woman who had completed ten pregnancies might, because of infanticide, rear no more children than a woman completing four pregnancies. It is interesting to contemplate the possibility that if this were the case, then by a very indirect means we may be returning to the same state of affairs. Family planning in this country increasingly converges on two or three children as an optimum (Freedman, Goldberg and Sharp, '55). With the wider dissemination of birth control information and education, the striking differentials in individual fertility shown in table 1 may tend to diminish appreciably in the near future. Indeed, there is evidence that this process has already begun.

The role of genetic drift in human evolution has been the subject of repeated speculation. The possible significance of drift in a population is inversely proportional to the effective breeding size of the population. Effective breeding size (N_e) was defined by Wright ('38) in terms of the number of parents in the population (N), and the variance in the average number of children (gametes) by which each parent is represented in the breeding population of the next generation (σ_k^2). To an approximation,[2]

$$N_e = \frac{4N - 2}{\sigma_k^2 + 2}.$$

In a sense, it is the significance of σ_k^2 which we have just been discussing. Since this term appears in the denominator of the expression which defines population size, factors decreasing its magnitude will increase effective population size. The trend in Western culture toward planned families of two to 4 children (cf. Freedman, Goldberg and Sharp, '55) thus has important implications for the concept of effective breeding population. Equally important is the increasing range of mate selection possible to the average individual, *i. e.*, the increase in N, which appears in the numerator of the expression defining effective population size. There are, then, two different factors at work today to increase effective

[2] This approximation holds only when the breeding size of the group remains the same in successive generations. However, departures from this condition only introduce another term in the expression.

population size and so to minimize the role of drift in human evolution. Drift which leads to the chance elimination of favorable genes is of course dysgenic. The obvious implication is that future populations will be more protected than primitive ones against one undesirable type of genetic change.

The effective breeding size of a human population is in actual practice difficult to define. This is well illustrated for a primitive population by the excellent study of Roberts ('56) on a Dinka village of the southern Sudan, and the equally excellent study of Spuhler and Clark (unpublished) on the somewhat less primitive population of Ann Arbor, Michigan. These difficulties notwithstanding, it is clear that the effective size of many primitive populations was small indeed, with the size subject to still further sudden and sharp decreases periodically because of the inroads of war, pestilence, and famine. Indeed, one who pursues these considerations is sometimes left wondering why the minor geographical subdivisions of the human race are not more strikingly different than they are. The answer perhaps lies in the apparently ceaseless migrations (and intermixtures) and custom-sanctioned exogamy of human populations.

Treatments of the dysgenic effects of ionizing radiation have thus far not taken into account the implications of the wide differences in individual fertilities. Two such implications in particular deserve mention. First, the probability of loss from the gene pool, which is already high for most recently mutated genes, will become even higher with such individual fertility differences as exist in human populations; on the other hand, the surviving newly mutated genes may undergo a relatively rapid increase in numbers, with a corresponding increase in the probability of homozygosity with respect to the mutant involved. For mutants with serious deleterious effects, the consequence would be an increased rate of elimination, with an earlier return to the equilibrium state than would be the case if each irradiated individual had the same chance of propagation. This consequence would appear to be of greater relative importance in small than in large populations. Second, to the extent that fertility is a nonspecific indicator of physical vigor, and to the extent that most nominal recessive mutants have slight heterozygote effects, it seems possible that in an irradiated population individuals who either by chance or by virtue of their radiation experience had accumulated significantly more mutant genes than the average might suffer from impaired fertility, and so fail to transmit their mutant genes to the next generation.

The Genetic Significance of Changing Dietary Patterns

The second area to be discussed as illustrative of the opportunities for the study of natural selection in human populations is concerned with changing dietary patterns and their relation to the pattern of morbidity and mortality in a population. We shall be forced to limit our considerations to a single cause of death, heart disease, the leading

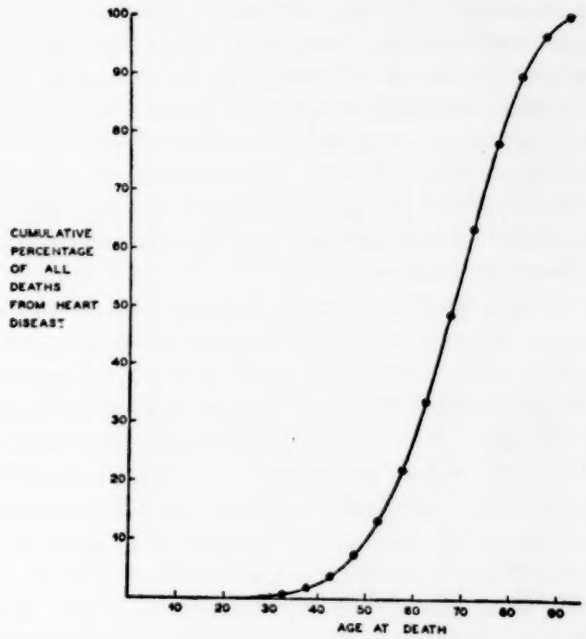

FIG. 1. CUMULATIVE FREQUENCY OF AGE AT DEATH FROM ARTERIOSCLEROTIC HEART DISEASE, NON-RHEUMATIC CHRONIC ENDOCARDITIS AND OTHER MYOCARDIAL DEGENERATION, AND HYPERTENSION WITH HEART DISEASE, IN THE STATE OF MICHIGAN FOR 1953. THE FIGURE IS BASED ON A TOTAL OF 20,546 DEATHS; THESE CONSTITUTED 33.1% OF ALL DEATHS IN THE STATE FOR THAT YEAR.

cause of death in the United States today. Figure 1 shows the age at death from arteriosclerotic, hypertensive, or " degenerative " heart disease in the state of Michigan for 1953. Some 3.7% of these deaths occur prior to age 44, and another 3.7% between the ages of 45 and 49. Moreover, hypertension, the predisposing factor in hypertensive heart disease, may result in relatively early death because of cerebral hemorrhage

or renal failure. In contrast, at least one of these important causes of severe heart disease, essential hypertension, is apparently much less common in many other cultures than in our own (review of literature in Bays and Scrimshaw, '53), and there is reason to suspect that one other cause of death from heart disease, arteriosclerosis (and its predecessor, atherosclerosis), may also be less common. The reasons for this have been extensively discussed; Murrill ('55) in particular has brought out the difficulty, on the basis of the existing data, of reaching conclusions concerning the relative importance of intrinsic (genetic) and extrinsic (environmental) factors in such differences as have been reported between various racial groups. In the following discussion, we shall not be concerned primarily with the question of genetic differences between racial groups in predisposition to various types of heart disease, but with the implications of changing environmental conditions on the expression and evolution of a given genotype. We shall limit our attention to two facets of the problem, namely, the effects of changes in dietary fat and salt intake.

Let us consider first the matter of dietary fat. By and large, in the world today the average intake of animal fat is proportional to the standard of living. Since the standard of living is rising, so also is the animal fat (and total caloric) intake; the relation of this to the apparent increase in coronary artery disease has provoked an extensive and controversial literature, which we cannot review exhaustively. As of this writing, the following statements seem justified: Individuals developing so-called coronary heart disease, including those in whom it appears at a relatively early age, tend to have somewhat elevated blood cholesterol levels, as well as altered phospholipid-cholesterol ratios (Davis, Stern and Lesnick, '37; Poindexter and Bruger, '38; Lerman and White, '46; Collen, '49; Adlersberg, Parets and Boas, '49; Gertler and Garn, '50; Gertler, Garn and Lerman, '50; Morrison, '52). These levels and ratios can be correlated with animal fat intake and altered by dietary measures (Dock, '50; Keys, Mickelsen, Miller and Chapman, '50; Hildreth, Mellinkoff, Blair and Hildreth, '51; Priddle, '51; Allen, Katz, Keys and Gofman, '52; Byers, Friedman and Rosenman, '52; Keys, '53; Pomeranze, '53; Keys and Keys, '54; Keys, Vivanco, Rodriguez Minon, Keys and Castro Mendoza, '54; Bronte-Stewart, Keys and Brock, '55; Keys, Anderson, Fidanza, Keys and Swahn, '55; Beveridge, Connell and Mayer, '56; Bronte-Stewart, Antonis, Eales and Brock, '56; Nelson, '56). There is evidence that serum cholesterol levels in individuals on the "average"

American or European diet are to a certain extent under genetic control (Wilkinson, Hand and Fliegelman, '48; Stecher and Hersh, '49; Adlersberg, '51; Schaefer, Drachman, Steinberg and Adlersberg, '53; Piper and Orrild, '56), although, for the milder degrees of hypercholesterolemia, the role of familial dietary similarities has not been properly investigated. It may thus be argued that diets relatively rich in animal fats (and generous in total calories) bring to light genetically determined differences in the ability to handle fat, differences which then become subject to natural selection. An additional (indirect) factor in bringing to light these differences may be the increasingly sedentary life of Americans, since a group of young individuals on a high fat, high calorie diet showed no elevation of serum lipoprotein and cholesterol levels as long as they exercised sufficiently vigorously to prevent weight gain, but did show such elevations in the absence of exercise and with weight gain (Mann, Teel, Hayes, McNally and Bruno, '55); but see Keys, Anderson and Aresu, '56). Thus, the greater physical activity of primitive man may have tended to keep his blood lipid levels low despite a diet relatively high in animal fat; this would help explain why selection has not previously operated on this system to a greater extent.

Most of the cholesterol in the blood is associated in complexes with proteins and lipids; there is a considerable range in the size of these molecular complexes. In persons with coronary heart disease there is a tendency for these molecular complexes to be larger than in persons without coronary disease (Gofman, Lindgren, Elliot, Mantz, Hewitt, Strisower, Herring and Lyon, '50; Gofman, Jones, Lindgren, Lyon, Elliott and Strisower, '50; Gofman, Glazier, Tamplin, Strisower and DeLalla, '54; Lyon, Jones, Graham, Gofman, Lindgren and Yankley, '52). These molecular complexes are also responsive to dietary measures such as restriction of animal fat (Lyon, Yankley, Gofman and Strisower, '56). Whether determinations of serum cholesterol levels or studies of lipoprotein molecule size have a greater predictive value as regards susceptibility to coronary heart disease is not yet clear (Committee on Lipoproteins and Atherosclerosis, 1956).

Genetic studies on the control of serum lipoprotein molecule size have yet to be carried out. However, it is difficult to avoid the speculation that increasing levels of animal fat consumption as well as an increase in total caloric intake, coupled with decreasing physical activity, have rendered important an agent of natural selection which formerly affected only a "favored" few. To the extent that there is a genetic determinant

in the ability to handle relatively high dietary fat loads without developing atherosclerosis, then biological natural selection should be at work in a society such as ours where one-fifth of the population over age 30, or about 15,000,000, are overweight, with an estimated 5,000,000 of these 20% or more above the ideal (Armstrong, Dublin, Wheatley, and Marks, '51).

You will have noted the emphasis on animal fat. This differs from vegetable fat chiefly in the greater degree of saturation or hydrogenation of the former. There is a growing body of evidence to indicate that the level of intake of vegetable fat has, on an equicaloric basis with animal fat, less tendency to elevate either serum cholesterol levels or the proportion of lipoprotein "macromolecules" (Kinsell, Michaels, DeWind, Partridge and Boling, '53; Ahrens, Blakenhorn and Tsaltas, '54; Beveridge, *et al.*, '56; Bronte-Stewart, *et al.*, '56). This statement holds true only for vegetable fats which have not been artificially hydrogenated, a practice now widespread because it renders some fats commercially more attractive. Hydrogenation, in increasing the degree of saturation of vegetable fats, reduces their content of the three so-called essential (unsaturated) fatty acids; these may play a role in the body's economy beyond that indicated by their degree of unsaturation alone (references in Rathmann, '57).

Let us turn now to the matter of salt intake. Until relatively recent times, salt was a rather precious commodity, with commerce in it often under government control. Today the salt consumption of the average individual in this country is probably 5 to 10 times greater than that of his counterpart in most groups of primitive man (Dock, '56). The role of this in the etiology of hypertension and hypertensive heart disease is debatable. However, it is a fact that rats placed on a level of salt intake equivalent to that of the average human diet will often develop hypertension (Meneely, Tucker, Darby and Auerbach, '53). It has also been reported that among 1,346 employees of the Brookhaven National Laboratory, the incidence of essential hypertension was significantly related to salt intake (Dahl and Love, '54, '56). There exist no data as to whether the ability to handle salt loads is at least in part genetically determined and hence susceptible to selection, but it would be surprising to me if it were not.

If, as mentioned earlier, heart disease of the types under discussion is uncommon in societies on a low-fat, low-salt diet, it will be interesting to observe the effects of a change in dietary habits on the morbidity

picture in these societies. For instance, there is some evidence that among primitive Africans blood pressures tend to be low, whereas among the American Negro hypertension is more common than it is in Caucasians (references in Bays and Scrimshaw, '53). Furthermore, it appears that certain categories of foreign-born students, coming to this country with relatively low blood pressures, over a ten-year period acquire blood pressures comparable with those of native-born Americans (Szent-Györgyi, '56). What is the role of altered salt intake in this difference? How does this relate to concomitant changes in the pattern of living?

Heart disease is but one of a number of disabling and potentially fatal diseases encountered in this country among young adults. For example, there are the so-called collagen diseases. Over the world, primitive peoples are being projected in a few generations from a Stone Age to an Atomic Age culture. In making this transition, they will be called upon to telescope into a few generations biological and cultural adaptations which have extended over a period of thousands of years in Europe. To the extent that these adaptations involve genetic systems, here is a priceless opportunity to study biological selection. One of the most exciting opportunities today is that of collaborative studies along these lines between anthropologists, geneticists, and physicians all over the world.

The Abnormal Human Hemoglobins

The third area to be discussed as illustrative of the opportunities for the study of natural selection in man, concerns the abnormal human hemoglobins. Our first example involved a situation where the genetic consequences are reasonably apparent, but the responsible genetic factors, if any, are quite obscure. In the second example, both the genetics of the situation and its consequences were somewhat better defined. We come now to what is probably the clearest opportunity existing today to analyze in detail a particular genetic system subject to a known selective pressure, and the potential consequences of a change in that selective pressure.

Even if time permitted, the number of reviews of the human hemoglobins which have appeared in recent years render any extended consideration of the basic facts unnecessary (White and Beaven, '54; Singer, '55; Itano, '55; Chernoff, '55; Itano, '56; Itano, Bergren and Sturgeon, '56; Zuelzer, Neel and Robinson, '56; Gatto, '56; Neel, '56, '57). The reader is no doubt aware that the sickling phenomenon is due to a gene

which when heterozygous produces a clinically asymptomatic condition known as the sickle cell trait, and when homozygous, the severe sickle cell anemia. In the sickle cell trait, 30 to 40% of the hemoglobin is of an abnormal type, known as hemoglobin S, whereas in the anemia, all the hemoglobin is of the abnormal type save for a fraction which may

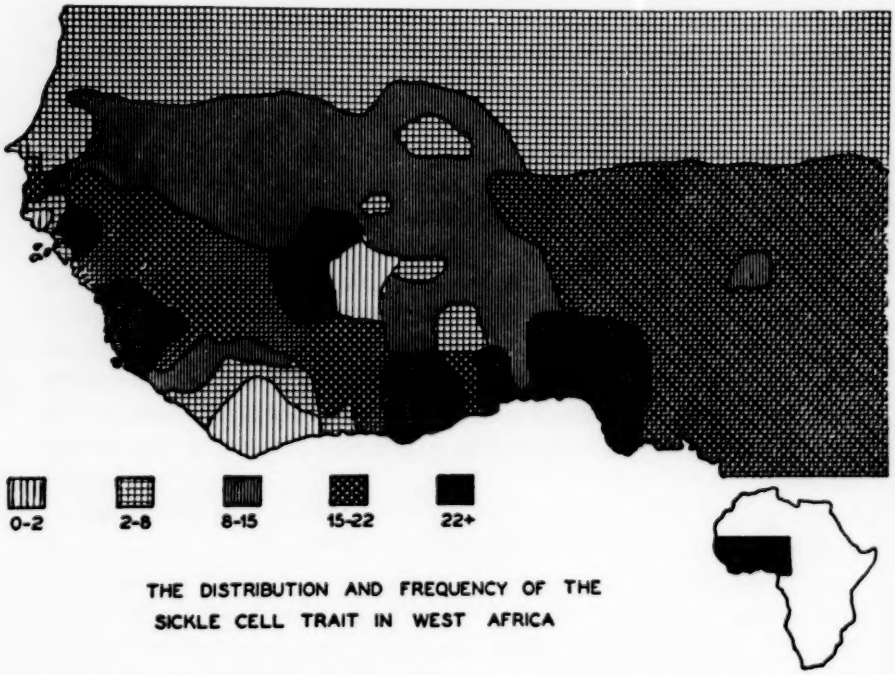

FIG. 2. THE DISTRIBUTION AND FREQUENCY IN WEST AFRICA OF THE SICKLE CELL TRAIT, MODIFIED FROM LIVINGSTONE, 1957. THE MAXIMUM FREQUENCY UNDER THE ENTRY "22 +" IS 31%.

be of the fetal type. A second abnormal hemoglobin also encountered in Negroes is known as hemoglobin C. Genetically, it behaves in the same way as hemoglobin S, but the disease state due to homozygosity for the gene is much less severe than in sickle cell anemia. The genes responsible for these two abnormal hemoglobins appear to be either alleles or linked. The known distribution and frequencies of these two genes in West Africa, in which we are particularly interested here, are shown in figures 2 and 3. These relatively high frequencies are probably maintained primarily through the mechanism of a balanced polymorphism.

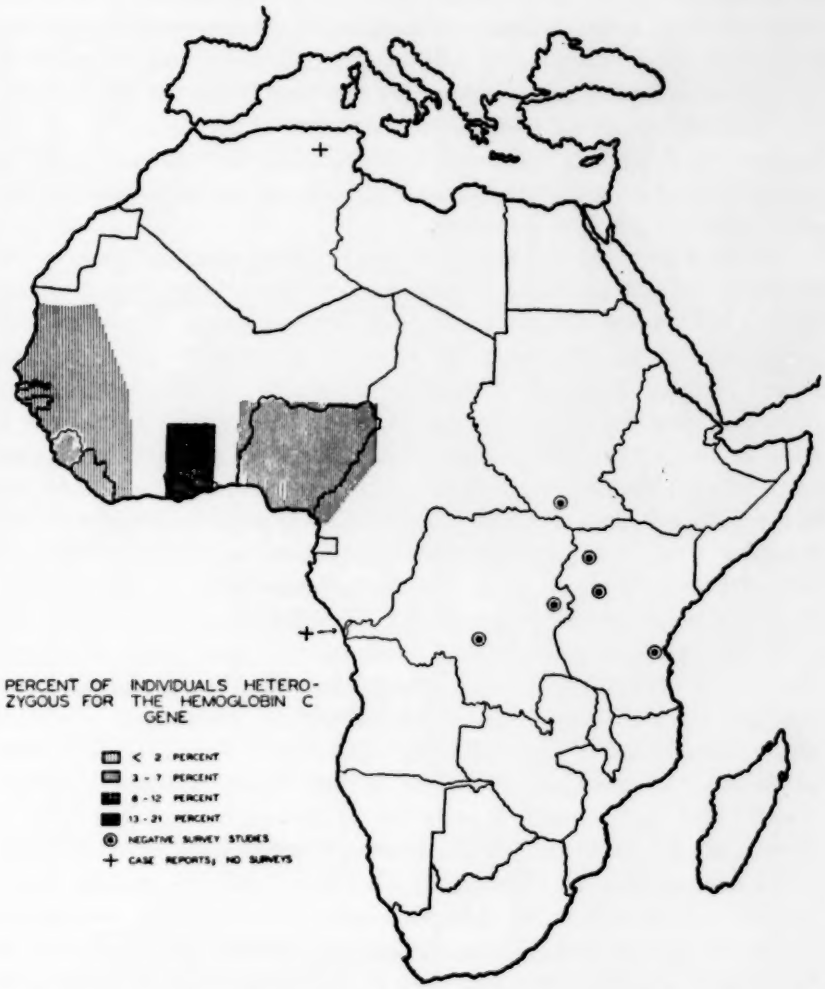

FIG. 3. THE DISTRIBUTION IN WEST AFRICA OF THE GENE RESPONSIBLE FOR HEMOGLOBIN C, AFTER NEEL, HIERNAUX, LINHARD, ROBINSON, ZUELZER, AND LIVINGSTONE, 1956 (reproduced by permission of the American Journal of Human Genetics).

The most plausible cause of this polymorphism yet advanced with respect to hemoglobin S is a lessened susceptibility of the individual with the sickle cell trait to the ill-effects of infection by *Plasmodium falciparum*. This thesis, so ably argued by Allison ('55), is undoubtedly familiar to the reader, but it seems unlikely that this constitutes the whole story. The mechanism responsible for the relatively high frequency of the hemoglobin C gene is unknown. Although the first possibility to be explored is again a differential susceptibility to malaria, data on this point have not yet been published.

All these facts are well known. There are some recent advances in our knowledge of the abnormal hemoglobins in West Africa which in my opinion open a new chapter in the study of these genes. There has been considerable speculation over the question of whether the sickle cell gene originated from one focus or multiple foci. This question may never be answered with finality. However, recent evidence makes it quite probable that in the western portion of West Africa at least, gene flow through migration supplies the major explanation of the distribution of the sickle cell gene, although the possibility of secondary, minor centers resulting from mutation and subsequent selection cannot be excluded with certainty. Our group has recently published data indicating a low frequency of the genes responsible for hemoglobins S and C among the tribes occupying the rain forests of southeastern Liberia (Neel, Hiernaux, Linhard, Robinson, Zuelzer and Livingstone, '56). Leite and Ré ('55) have also reported a low frequency of the sickling phenomenon in certain of the tribes found in Portuguese Guinea. Figure 4 indicates one interpretation of the areas of distribution in West Africa of tribes exhibiting a sufficiently distinctive and primitive culture to be regarded as more directly related to the early inhabitants of West Africa than many of the tribes now residing in that region (Baumann and Westermann, '48). It will be noted that of the three such areas in West Africa, two involve Portuguese Guinea and Liberia. On the basis of these facts, Leite and Ré have urged that the sickle cell gene is a relatively recent introduction into western West Africa, a point of view with which I agree. Otherwise stated, while the possibility of the origin of the sickle cell trait through mutation in West Africa cannot be excluded, there is evidence for a very substantial influx of the gene in consequence of relatively recent migratory flow originating east of the Gold Coast.

If we accept the point of view that the sickle cell gene owes its presence in western West Africa in whole or in part to an introduction

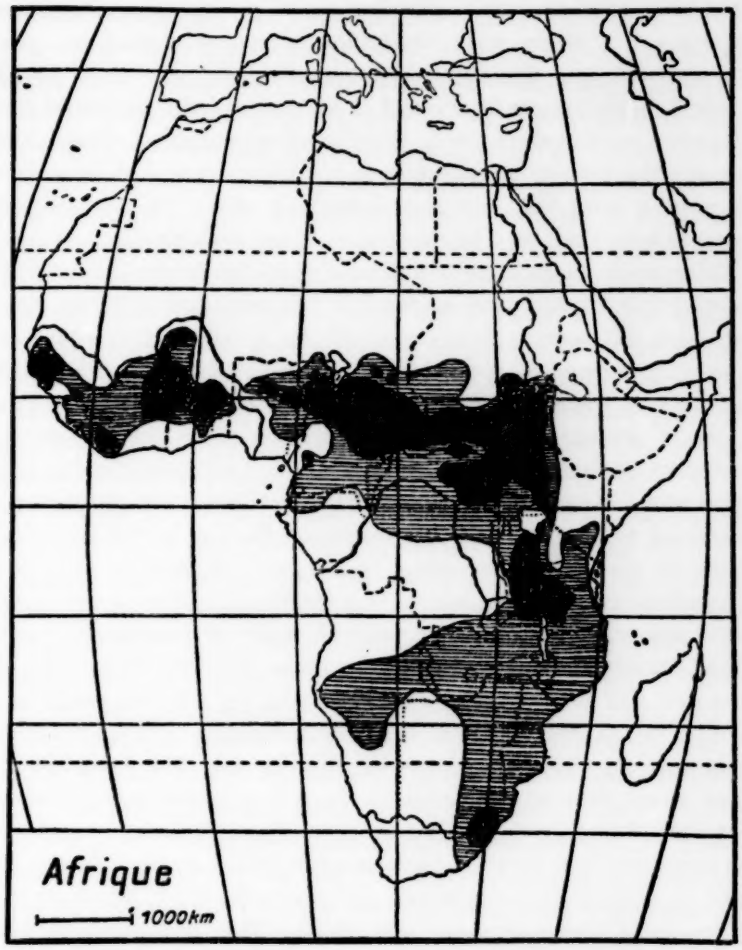

FIG. 4. THE DISTRIBUTION OF "PALEONEGROID" ELEMENTS IN AFRICA. This figure is reproduced by kind permission from "Les Peuples et les Civilisations de l'Afrique," by H. Baumann and D. Westermann, published by Payot, Paris, 1948.

in the not-too-distant past, then some very obvious questions at once arise regarding the distribution of hemoglobin C. The "diffusion gradient" type of frequency distribution shown by this gene implies a relatively recent origin, with dissemination from a single focus. Is this origin pre- or post-migrational with respect to the sickle cell gene? If the origin is post-migrational, and if the time of the migration can be even approximately established, there is an unparalleled opportunity to document the date of appearance and subsequent spread of a "new" human gene with the resulting inferences about its selective value, inferences which can then be checked by direct observation.

There would seem to be two chief approaches to the question of the time of origin of the gene responsible for hemoglobin C. On the one hand, some information should come from a detailed study of the distribution of the gene in West Africa. As pointed out elsewhere (Neel, *et al.*, '56), if the origin of the gene is essentially pre-migrational, then one might expect a "tear drop" distortion from the pattern to be expected of radiation from a central focus. The precise nature of the pattern to be expected depends on many variables, but the gene might be expected to occur with a low frequency further to the west than to the east of the area of maximum frequency. The present sketchy data are insufficient for an opinion on this point.

The second approach to the time of origin of the gene depends on detailed anthropological studies of the tribes with the highest frequency of the gene. If they are otherwise essentially no different from the surrounding tribes, this suggests a post-migrational origin. But if they are set apart by characteristics which, for example, link them with older human strata, then one is forced to visualize a migratory current which swept around and by them. Returning to figure 4, we note an approximate correspondence between the area of highest frequency for the hemoglobin C gene and the third of the areas in West Africa in which "paleonegroid" elements are prominent. This latter is the "Niger circle" area, into the western portion of which there seemed to have been compressed a number of relatively primitive and thus far poorly studied tribes.[3] However, although the coincidence is certainly apparent, it should be emphasized that the area is large and that only a few of the tribes involved have been sampled thus far. The present evidence, then, is at least consistent with the view that the origin of hemoglobin C

[3] I am indebted to Dr. Frank Livingstone for a great deal of helpful discusssion concerning the anthropology of West Africa.

may well be pre-migrational with respect to the sickle cell gene—but sufficiently recent that the gene had not yet had the opportunity to diffuse extensively throughout the "paleonegroid" tribes of West Africa. An alternate possibility, based in part on the evidence that a number of the tribes of West Africa show a complementary relationship between the frequencies of the S and C genes, with the appropriately weighted sum of the two approximating a constant (Allison, '56), would be that the C gene had arisen post-migrationally and is in the process of displacing the S gene. The differentiation between these two possibilities rests in large part on intensive study of the little known primitive tribes of the Niger circle. If, in tribes which by all standards have the smallest infusion of genes from later migrants into West Africa, the sickle cell gene is either absent or present in low frequency while the C gene is relatively frequent, the most logical explanation would seem to invoke an origin of the C gene prior to the introduction of the S gene. This, of course, does not rule out the possibility that where the two genes overlap in their distribution, C will now displace S.

One further development should be mentioned. With the conditions under which paper electrophoresis is usually carried out, most of the abnormal hemoglobins migrate more slowly than normal, but American investigators have recently described three new and rapidly migrating hemoglobins, each on the basis of the findings in a single family. These are termed H (Rigas, Koler and Osgood, '55), I (Rucknagel, Page and Jensen, '55) and J (Thorup, Itano, Wheby and Leavell, '56). We have found in Liberian natives two rapidly migrating hemoglobins, one occurring in 7 out of 920 individuals, the other in two out of 920 individuals (Robinson, Zuelzer, Neel, Livingstone and Miller, '56). The more frequent of these corresponds to hemoglobin J, which in thousands of electrophoretic studies on randomly selected American Negroes has thus far been encountered in only one individual. The other hemoglobin appears to be distinct from both H and I, and hence to be a new one. Independently of the American investigators, Cabannes and his collaborators have described two rapidly migrating hemoglobins in blood specimens from Algerian natives (references in Cabannes, Duzer, Portier, Massonnat, Sendra and Buhr, '56). Neither of these corresponds to hemoglobin H, but their relation to I, J, or the new hemoglobin encountered in Liberia is not clear. In a sample of 1,624 hospitalized Algerians studied by Cabannes and his collaborators, there were 4 individuals with one of the fast components and one with the other, while 0.9% had hemoglobin

C either alone or in combination with A or S, and 0.5% had hemoglobin S, alone or in combination with A or C (Cabannes, *et al.*, '56). The finding of S and C in these relative proportions suggests that the Negro admixture in the North African native may, on the basis of the hypothesis discussed above, involve a higher proportion of the paleonegroid stock than of the more recent arrivals. Furthermore, if the fast-moving hemoglobins encountered in North Africa prove to be the same as were found in Liberia, then it may be postulated that these hemoglobins will in time be discovered in some of the tribes of the French Sudan, a finding of importance in understanding the biological relationships of the tribes of this area. Thus, since Cabannes *et al.* encountered fast-moving hemoglobins most frequently in the Kabyle Berbers, we may speculate that these hemoglobins will be found in the Tauregs and related peoples of the French Sudan; if the fast hemoglobins encountered in Liberia prove similar, a very interesting pattern of gene exchange in prehistoric times will emerge. In this connection, it should be noted that in the tribe with the highest proportion of individuals exhibiting hemoglobin C yet studied (26.8% in 71 northern Gold Coast Dagomba; Edington and Lehmann, '56), no examples of a rapidly migrating hemoglobin were encountered.

Finally, on the assumption that the malaria hypothesis supplies the principal explanation of the high frequency of the sickle cell gene, let us consider briefly the consequences of malaria control in Africa. Such control must lead to a decrease in the frequency of the gene, in a perfectly predictable manner worked out by Smith ('54). For the time being, this is probably the clearest example in all human genetics of the effect of an environmental change on the future evolution of man.

The abnormal hemoglobins represent but one of a number of situations where there are marked gene frequency differences between racial groups. The findings regarding the various inherited serotypes at once come to mind. Although at one time there appeared to be a sharp difference in the population genetics of the "unfavorable" hemoglobin genes and the more nearly "neutral" serotype genes, we must now, as I pointed out a few years ago (Neel, '54), recognize a continuity of problem. There are decreasing grounds for regarding the situation typified by the hemoglobin genes as a genetic curiosity, clearly to be distinguished from the more orthodox behavior of the genes producing serological reactions. Rather, in the hemoglobin genes we are confronted with a tactically favorable situation from which may emerge answers of uni-

versal applicability. With respect to quite a number of human genes which, because of their frequency, distribution, and clear-cut effects are favorable material for studies on selection, we find ourselves in something of the same position as virologists interested in the large group of adenoviruses. These are sometimes called the " orphan " viruses, since so many of them have not yet been related to specific diseases. So, also, for many of the known human genes we have yet to acquire an appreciation of the range of their effects. If recent studies on the relation between ABO blood groups and duodenal ulcer are correct in suggesting that an important factor may be the blood group of the mother of the affected individual (Clarke, Edwards, Haddock, Howel-Evans, McConnell and Sheppard, '56), this provides an interesting insight into the complexity of some of these selective relationships. Further insight into the undoubted complexity of these problems is provided by the relationship of ABO blood type to the probability of Rh isoimmunization (Levine, '43; Van Loghem and Spaander, '48) and the role of the secretor factor in the development of duodenal ulcer in a blood group O individual (Clarke, *et al.*, '56).

SUMMARY

We have briefly surveyed three areas in which the time seems propitious for work on natural selection in human populations. Other areas will undoubtedly occur to the reader. The study of the means whereby human populations rid themselves of undesirable genes and conserve those advantageous to the species is scarcely underway. Not until we are in command of such information can we truly understand man's past or predict his future in a rapidly changing world.

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SOMATOTYPE AND SEXUAL MATURATION IN BOYS: A METHOD OF DEVELOPMENTAL ANALYSIS

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IN a previous paper, the senior author mentioned the desirability of describing the typical trajectories of physical growth and development of individuals of different body builds (Hunt, '52). In the present study, such trajectories have been calculated from data on a succession of stages of sexual maturation in boys. These findings were obtained during a growth study under the direction of one of us (J. R. G.), which was carried out from 1939 to 1942 on a group of boys attending a boarding school in New England. Information was utilized on their ages, somatotypes, and degrees or stages of sexual maturation. As used here, the data are wholly cross-sectional.

In order to arrive at these developmental trajectories, the senior author devised a chronological method of describing sequences of stages of human maturation. This procedure can be used whenever ratings of somatic development are available for a sample of children of various ages. The technique is based on elementary concepts of statistics and logarithms and has both versatility and generality. One can readily compute the variability of a group of children in attaining the stages of maturation, a developmental age equivalent for each stage, and at any desired age, the incidence of children in the population who are within the different stages.

If stages of development have been assessed for several distinct tissues or organs in a group of children, this method makes it possible to determine the degree of integration or unity of maturation of these structures,

even where the sequence of appearance of the stages may vary from one child to another.

Within a total series of children, this procedure also permits the comparison of subgroups with one another. The chronology of the total series is considered to be normative with respect to variability, earliness or lateness of maturation (timing), and the velocity of passing through the stages. By further calculations, these three measurements of each subgroup are compared with those of the total series. Alternatively, these three measures from two separate samples of children can be compared with one another.

Variability, timing and velocity add up to a relatively complete description of a developmental trajectory in a group of children. In the present study of physique and sexual maturation, data of this kind seem to indicate a mechanism at the basis of sexual development which might well be studied experimentally.

The Theory of Normative Developmental Chronologies

For the entire series of boys, the chronology of their sexual maturation was based on what we call *attainment curves.* An attainment curve is a distribution representing the percentages of individuals who have *attained or surpassed* any particular stage of maturation, as plotted against either their chronological or their developmental ages.

Even the simplest graphic attainment curves often yield insights into growth and development. Notable in this respect are studies of the attainment curves of the emergence of teeth in man by Hurme ('48) and in the rhesus monkey by Hurme and van Wagenen ('53, '56). " Emergence " in this case refers to the brief period during the eruption of a tooth when its crown first perforates the gingival mucosa.

In general, such emergence curves are positively skew cumulative frequency (ogive) distributions, as shown in figure 1a. The data for figure 1 are based on the emergence of the deciduous mandibular central incisor in Boston White infant girls, as published by Doering and Allen ('42).

Because of the skewness of these distributions, the median age of emergence of a tooth is somewhat younger than the mean. Furthermore, the age range from the first percentile to the median, for example, is shorter than the interval from the median to the 99th percentile (Hurme, '48). It is therefore desirable to modify the widths of the class intervals of the age axis in order to eliminate this skewness.

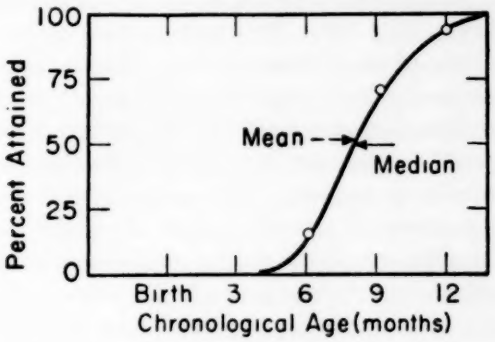

FIG. 1A. ORIGINAL ATTAINMENT CURVE (SKEWED).

Kihlberg and Koski ('54) found that when the age axis is transformed into a logarithmic scale, such skewness disappears because the lower half of an attainment curve is stretched along the age axis, and the upper half is contracted. As shown in figure 1b, a semilogarithmic plot of an attainment distribution produces a symmetrical ogive. As will be seen presently, this new curve is also normal.

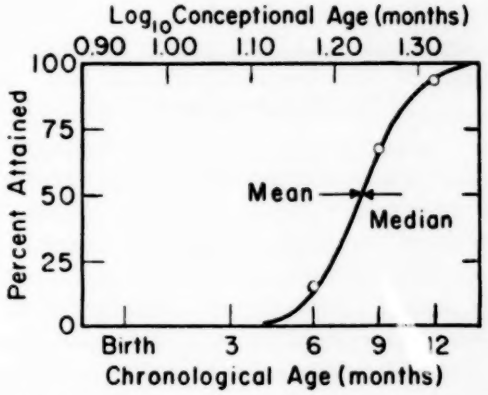

FIG. 1B. AGE AXIS TRANSFORMED AND SKEWNESS ELIMINATED.

For most purposes, the most suitable logarithmic transformation of age scales is the approximate interval of time from conception to the date of observation (Kihlberg and Koski, '54). In man, this so-called " conceptional age " is usually taken as age from birth plus the traditional average human gestation period of 9 months. A slightly more accurate

estimate of the mean gestation period would be 8.9 months, or 0.74 year (Hotelling and Hotelling, '32). This value is used in the present study. Where the true date of conception is known, however, the exact conceptional age can be used (Hurme and van Wagenen, '56).

In any logarithmic transformation, the earliest log cycles have a total breadth which approaches infinity. In studies of infants, it is therefore undesirable to consider birth as the origin of coordinates of the age axis and far better to use conception. By this device, the problem of inordinate breadths of the early log cycles occurs only before the blastocyst is implanted in the uterine wall. The scale of log conceptional age makes it easy to study the continuity of fetal and postnatal growth.

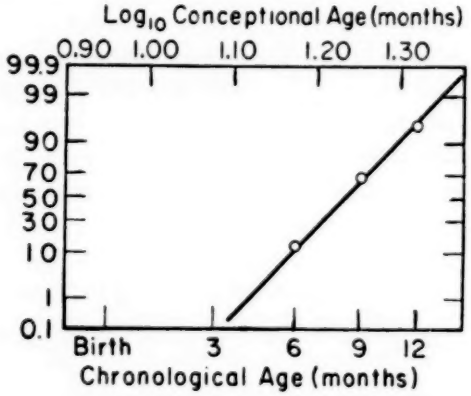

FIG. 1c. PERCENTILE AXIS TRANSFORMED (LOG PROBABILITY GRAPH) TO PRODUCE LINEAR ATTAINMENT CURVE.

For the convenience of the reader, it is often desirable to label the postnatal intervals of this scale by chronological age. Jennings and Pyle ('55) have used such a relabeled scale extending from birth through adolescence in their "Merrill-Palmer logarithmic developmental graph." This graph can be used to relate developmental and chronological ages in individuals or groups of children.

The S-shape of a normal ogive plot of percentiles on log conceptional age can be transformed into a straight line if the upper and lower ranges of percentiles are properly stretched at the extreme values (figure 1c). In precise terms, consider a scale where the 50th percentile equals zero, and which is positive at higher percentiles and negative at lower ones. The percentiles are converted into standard deviation units by means of

a table of areas under the normal curve. For example, the standard score + 1.00 is at percentile 84.13, and — 1.00 is at the 15.87th percentile.

The correct spacing of the percentiles and log age units are built into the so-called "log probability" graph paper, which may be purchased from the Codex Book Co., Norwood, Mass. On this paper, the user records the chronological age units at intervals on the log axis for conceptional age. He then plots the percentages of individuals in various age groups who are at or beyond a given stage of development and connects these points with a line, as shown in figure 1c.

A succession of linear attainment curves can readily be drawn on one graph, and the line for the terminal stage characterizes only the *attainment* of this final level of development. If interest centers on the maturation of several distinct organs, such as different classes of teeth, attainment curves from these diverse sources can be plotted on one graph.

If consideration is limited to one developing organ, its family of attainment lines must *necessarily* be parallel if all the stages are clearly separable and irreversible in their sequence. If a line were not parallel with its neighbors in the sequence, it would intersect with them, and at percentiles beyond these intersections, the stages would be erroneously reversed.

At the Forsyth Dental Infirmary for Children, Miss E. A. Fanning has made extensive tests of this expectation of parallelism in radiographic studies of dental development. This statistical phenomenon occurs in the stages of calcification of a tooth, and also in the stages of resorption of roots of deciduous teeth.

An important test of parallelism is whether it occurs in the development of separate tissues or organs. Where it does exist, these structures apparently mature in a systematic or integrated relationship with one another, but not necessarily in an irreversible sequence. The further exploration of such a system would involve correlations between the standard scores of attainment in the development of the different organs, and tables of the incidences of the various alternative sequences of stages in the population.

The occurrence of parallelism in the development of several organs seems to have been first demonstrated by Kihlberg and Koski ('54). These authors found that different classes of teeth in some instances exhibit parallelism in their curves of clinical emergence in both man and the rhesus monkey. We have made plots of the succession of developmental stages of pubic hair and genitalia in boys, as published by

Reynolds and Wines ('51), and found that the attainment curves of these two tissues are parallel. The same is true of the three attainment lines for initial breast development, first pubic hair and menarche in girls, based on data from Reynolds and Wines ('48).

An algebraic treatment of parallel attainment equations reveals some of their very useful statistical properties. Let c represent a positional constant which is distinctive for the equation of each stage in a succession. For all the equations of the sequence, z represents the standard score of the percentile of individuals at or beyond a given stage, t equals conceptional age, and a equals a constant. All the parallel lines will then assume the form:

$$z = a \log t + c.$$

All of the attainment equations will have identical slopes, and this slope is also the standard deviation of each attainment distribution in units of log conceptional age: i. e.,

$$\sigma_{\log t} = \frac{1}{a}.$$

In an irreversible sequence of parallel attainment lines, let us determine what "developmental age equivalents" should be assigned to stages which are transitory or intermediate states of the organism. For any such stage, we define a segment of the $\log t$ axis, extending from the mean age of attainment of the stage to the corresponding mean of the next succeeding stage. The midpoint of this segment is the "midpoint age."

Consider a theoretical population, all members of which are at the midpoint age. Half of these individuals will be *in the middle of, or beyond* this developmental stage. Still more important, at this age, the incidence of individuals *at or within* the stage is maximal. Thus, the midpoint age is simultaneously a mean, median and mode, and is therefore a proper developmental age equivalent of the stage.

In publishing growth data, one may need a frequency distribution of individuals who are within a stage. For this purpose, we merely require a bell-shaped normal distribution with a mean at the appropriate midpoint log conceptional age and a logarithmic standard deviation of $1/a$.

The maximal incidence of individuals at the midpoint age is calculated by substituting the midpoint age in units of $\log t$ into the equations of the two adjoining attainment lines and solving each equation for z.

These two standard scores are then converted into percentiles, and the percentile for the later stage is subtracted from that of the preceding one.

Calculations of incidences can of course be produced for any desired age. To find the incidence of individuals who have not yet entered the sequence, we subtract the percentile of the least mature stage from 100%. The percentile for the terminal equation gives the incidence at this age who have completed the sequence. The difference between the percentile of attainment of any intermediate stage and the next succeeding percentile represents the incidence within the stage. By such steps, it is easy to prepare a table of incidences for any desired set of ages from a log probability plot.

The Theory of Group Comparisons

In considering the pattern of development in an arbitrary subgroup taken from a total series of individuals, we calculate a family of attainment equations for the subgroup alone. In this case, the standard deviation of ages of attainment ($\sigma_{\log t}$) of the subgroup is compared with the corresponding normative standard deviation for the total series. Such a comparison indicates whether the subgroup is more or less variable than the total series in its maturation.

For the additional comparisons of the subgroup with the total series, we employ the method of allometry. In a series of organisms which vary in size and shape, allometry is the use of equations which portray the relationships between the logarithms of two somatic measurements or biochemical determinations (Smith, '54; Hunt and Giles, '56). In the present study, however, the method involves the comparison of two sets of mean logs of conceptional age of attainment of a sequence of maturational stages. For our allometric equation, y represents the mean conceptional ages of attainment for the total series and x those of the subgroup. Log b is a positional constant and k is the coefficient of relative growth. The equation is in the form:

$$\log y = k \log x + \log b.$$

Since this equation characterizes an allometry of time rather than of metrical data, the constant $\log b$ is not a mere artifact of the units of measurement. Instead, the sign and value of $\log b$ help to show the *timing* of sexual maturation in the subgroup. Where $\log b$ is negative and k is close to unity, the subgroup is consistently late in maturation. Where k is close to unity and $\log b$ is positive, a subgroup is consistently

early in maturation. Where k diverges far from unity, however, the interpretation of k and $\log b$ is likely to be more complicated.

The k coefficient measures the *velocity* of maturation typical of the subgroup. Where $k = 1.25$, for example, the subgroup has traversed its developmental sequence 25% faster than the total series. If $k = 0.75$, on the other hand, the development of a subgroup is only 75% as fast as the average for the total sample.

As will be seen later, a satisfactory computational technique for the present data remains for the future, and as used here, the comparisons are admittedly crude. The biometrician will see that confidence limits and tests of significance for the various statistics of the attainment curves would be highly desirable.

The testing of parallelism in an assortment of attainment equations is not unlike the evaluation of parallelism in the slopes of equations of dosage responses in bioassay investigations (Bliss and Calhoun, '54). The closest analogy is the replication of assays of a single unknown biological substance as compared with a standard substance. The simplest fiducial test of parallelism of attainment curves would be based on cross-sectional data such as the present materials on adolescent boys. Adapting the test to semi-longitudinal or fully longitudinal data, however, would probably not be easy. A beginning might be made in such cases along the lines suggested by Tanner ('51) for metrical data.

The present method of comparison need not be limited to a subgroup as related to a total series. An even more important application might be the comparison of two or more distinct groups of individuals—especially when one group served as a reference or normative standard of development. On the basis of the normative sample, the variability, timing and velocity of development of the other groups could be conveniently recorded and interpreted.

The Calculations for the Total Series

Greulich *et al.* ('42) published data on the percentages of boys who were within a series of stages of maturation of the genitalia and body hair in age classes ranging from 12 to 17 years. These findings were based on 476 boys from the same boarding school as the smaller series used here. On log probability paper, we found that the attainment curves for these stages were straight parallel lines. These lines were not fully precise, however, because the midpoints of the age-class intervals were not specified.

The basic stages of maturation are 5, and a boy can be assigned either to a basic stage, or to an intermediate stage such as 1-2, 2-3, 3-4 or 4-5. This elaboration gives a full complement of 9 stages. The 5 basic stages are described in detail by Greulich *et al.* ('42). In brief, they are as follows:

1. External genitalia small as in a young child; body hair unpigmented vellus only.

2. Testes usually enlarged; long, downy, slightly pigmented hair present at base of penis.

3. Penis definitely enlarged; first coarse, fully pigmented pubic hair; often first lightly pigmented facial hair.

4. Further enlargment of penis and testes; pigmented hair not yet present on thighs or lower abdomen; coarse facial hair present, especially on upper lip, in front of ears, and chin. Circumanal and axillary hair usually well developed.

5. Penis and testes at nearly adult size and sometimes disproportionately large. Public hair usually as in the adult in quantity and type. Coarse pigmented hair present in hairy individuals on thighs and linea alba. Variable amounts of coarse terminal hairs on upper lip, chin, and sides of face. Circumanal and axillary hair well developed.

These stages were rated by personal inspection of the individual boy by Greulich.

Of the 476 boys in the entire growth study described by Greulich *et al.* ('42), 226 had not only been assigned to the preceding basic or intermediate stages, but had also been somatotyped by C. W. Dupertuis. The ratings of physique were performed from body build photographs according to the inspectional technique of Sheldon *et al.* ('40).

The present authors utilized this lesser sample in computing a normative set of parallel linear attainment equations. The earliest equation is for boys at or beyond the onset of pubescence (stage 1-2), and the 8 remaining equations apply to the subsequent basic and intermediate stages.

The 226 boys ranged in chronological age from 13.08 to 17.58 years when their maturation was rated. Within two months of this occasion, each boy was photographed for somatotyping.

For computational purposes, the series was separated into younger and older groups at the 15th birthday on the basis of the age at which maturation had been rated. For each group, the percentage of boys at

or beyond each stage was found. These percentages were then converted into standard scores from a table of areas under the normal curve.

For the time axis, the age when each boy was given his maturational rating, was converted into the $\log_{10}$ of conceptional age. For the younger and older age groups, the means of the logs of conceptional age were found. The two means are the age-coordinates for the arrays of standard scores of attainment.

In order to find the common slope or standard deviation of the attainment curves, a bivariate distribution was set up of all the standard scores of percentages of attainment within the limits 0 — 100%. The stages within these limits in both the younger and older groups were 3-4, 4, 4-5 and 5. A least-squares regression of z on $\log t$ was computed to arrive at a value of a for these 4 stages. The reciprocal of this value was then the common slope or standard deviation ($\sigma_{\log t}$) for these 4 stages. The remaining step was to calculate c for each separate attainment equation.

In the younger group, percentages of less than 100% were available for stages 1-2, 2, 2-3 and 3. Log t was fixed at the mean age for the younger group, as described earlier, and a was the constant which had been derived in the preceding least-squares computations for the later stages. Substituting the appropriate z score for each early stage into the basic linear equation along with $\log t$ and a, the corresponding value of c was found.

For stages 3-4, 4, 4-5 and 5, the values of c were computed by substituting the constant value of a into the two normal equations which are customarily used for least-squares estimations. Where N represents the number of z scores used (two in all the present cases), the first normal equation was

$$\Sigma z = Nc + a \Sigma \log t.$$

This value of c characterizes an attainment equation which crosses the centroid of the two loci of the z scores.

The second estimate of c, from the other normal equation, is the least-squares line of regression of z on $\log t$. This equation is

$$\Sigma z \log t = c \Sigma \log t + a \Sigma (\log t)^2.$$

As shown in table 1, the centroid and least-squares estimates of c agree closely except for stage 4-5. This agreement is indicative of the suitability of the system of parallel lines as a fit for the present data,

and the mean of the centroid and least-squares estimates for each equation is used for the later computations in this paper.

Calculations for the Somatotype Subgroups

The 226 boys in the present series were divided into 6 subgroups according to their dominance of one, or balance of two or three, of the somatotype components. For each subgroup, parallel attainment equations were computed as for the total series. One small subgroup (the balanced endo-mesomorph class) had to be omitted from consideration because its younger array was more advanced in maturation than its older one. All that could be done with this omitted subgroup was to find the incidence of stages at the mean log conceptional age of the whole undivided class.

The values of a for the large samples of dominant mesomorphs and dominant ectomorphs were based on stages 3-4, 4, 4-5 and 5. The smaller samples with balanced mesomorphy and ectomorphy, and with equality of all three components, have this coefficient based on stages 4, 4-5 and 5. The smallest usable sample (the endomorphs) has a value of a based on stages 4-5 and 5 only.

As in the total series, the values of c for some of the earlier stages were found from the value of a for the combined later stages, together with the appropriate computations of z and $\log t$ for each younger array of boys. For the separate later stages, the centroid and least-squares values of c were calculated as for the total series.

For each subgroup, the standard deviation ($\sigma_{\log t}$) expresses the degree of individual variation in attainment of the stages. The $\log t$-intercepts of its family of attainment curves provide a set of mean log conceptional ages which can be compared with their equivalents for the entire series by the method of allometry.

Each of the allometric equations was computed by the simplest reduced major axis method of Kermack and Haldane ('50) from the mean conceptional ages of attainment for the total series (y) and the corresponding means of each somatotype subgroup (x). Letting $n =$ the number of pairs of means utilized:

$$k = \frac{\sigma_{\log y}}{\sigma_{\log x}} \text{ and } b = \frac{\Sigma \log y - k \Sigma \log x}{n}.$$

FINDINGS ON THE TOTAL SERIES

The chronology of attainment of the maturational stages of the total series is shown in table 1, and graphed in figure 2.

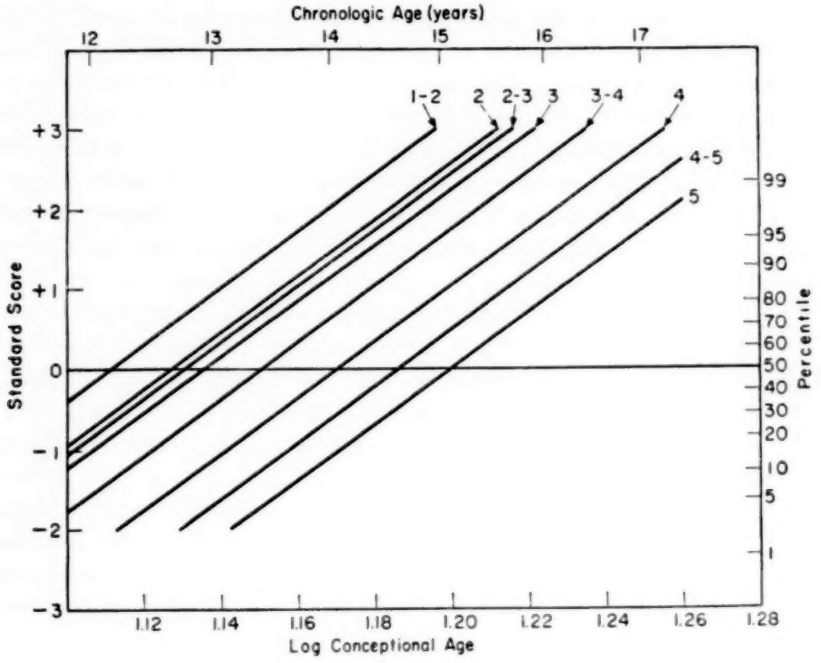

FIG. 2. ATTAINMENT CURVES FOR SEXUAL MATURATION OF 226 PREPARATORY SCHOOL BOYS.

In these boys, the variability of attainment of the stages ($\sigma_{\log t}$) is 0.029 log units. We have analyzed attainment curves from longitudinal data published by Reynolds and Wines ('51) on 4 stages of pubic hair and 4 of the genitalia in boys from the Fels Institute growth study at Yellow Springs, Ohio. All 8 of these equations, too, are parallel and have a variability of attainment of 0.029 log units. This agreement indicates the soundness of the present computational method, even though it is based on cross-sectional data on a restricted portion of the age range of normal adolescent development.

The mean of the first attainment curve in our sequence (stage 1-2) or the onset of pubescence, is at 12.20 years. This estimate is slightly later

TABLE 1

Attainment equations for stages of sexual maturation in 226 preparatory school boys

STAGE	c			LOG t-INTERCEPT (50TH PERCENTILE)			MEAN CHRONOLOGICAL AGE IN YEARS		
	One locus	Centroid	Cross-products	One locus	Centroid	Cross-products	One locus	Centroid	Cross-products
1 — 2	— 38.6786			1.1115			12.20		
2	— 39.2486			1.1279			12.69		
2 — 3	— 39.3536			1.1309			12.78		
3	— 39.5286			1.1360			12.94		
3 — 4		— 40.0174	— 40.0153		1.1500	1.1500		13.39	13.39
4		— 40.6974	— 40.6989		1.1700	1.1700		14.05	14.05
4 — 5		— 41.2424	— 41.2011		1.1852	1.1840		14.58	14.54
5		— 41.7374	— 41.7375		1.1994	1.1994		15.09	15.09

z = standard score of % boys at or beyond stage.

t = conceptional age in years.

Basic equation: $z = 34.7973 \log t + c$.

than the onset of genital maturation in Tanner ('55), but close to the onset of pubic hair development. This finding suggests that on a cross-sectional basis, an observer can judge the initiation of pubic hair development more accurately than the first enlargement of the testes. Pubic hair is either visible or absent in a boy: whereas an observer may be uncertain whether the testes have begun to enlarge unless he has a recent prior body build photograph of the same boy as a standard of reference.

Greulich's stage 3, which includes the first appearance of coarse and fully pigmented pubic hair, is attained at a mean age of 12.94 years in the present series and at just over 13 years in the compilation of Tanner ('55). This agreement is again quite satisfactory.

The final stage in Greulich's chronology, stage 5, is not the true end point of sexual maturation. It is "open-ended," and the mean age of attainment is 15.09 years. This age is much younger than the terminal stages of sexual development as found from serial photographs and personal inspections of boys, especially those of Stolz and Stolz ('51) and Reynolds and Wines ('51). We see no reason, however, to consider this divergence as anything but an artifact in the definition of stage 5. Phenomena such as the shrinkage of the penis in the late teens, as documented in many boys by Reynolds and Wines ('51), would be very difficult to rate on a cross-sectional basis.

FINDINGS ON PHYSIQUE AND MATURATION

The statistical data relating somatotype and sexual maturation in the present study are presented in table 2, and in graphic form in figure 3.

The *timing* of maturation is consistently early in dominant mesomorphs, as noted by Tanner ('55) and others. This finding is nearly as true of the balanced mesomorphic-ectomorphic subgroup as of the heavier muscular individuals. As mentioned earlier, the balanced endomorphic-mesomorphic subgroup was unsuitable for a full mathematical treatment, but of the 15 boys in this small sample, 67% were at stage 5, while the predicted incidence at the equivalent mean log conceptional age in the total series of 226 boys would be 46%.

The *variability* of maturation in the somatotype groups shows a fairly consistent association with the percentage of fat in the body. The leanest group (ectomorphs) have a low variability. The groups with midrange fat content are in the midrange of variability, and the most adipose boys

TABLE 2

Variability and allometric constants of sexual maturation in somatotype subgroups

GROUP	N	VARIABILITY OF ATTAINMENT OF STAGES	ALLOMETRIC CONSTANTS COMPARING SOMATOTYPE SUBGROUP WITH TOTAL SERIES	
		$\sigma_{\log t}$	k	b
Total series	226	0.029	——	——
Dominant endomorphs	16	0.033	0.822	+ 0.207
Dominant mesomorphs	91	0.032	0.932	+ 0.085
Dominant ectomorphs	59	0.021	1.442	— 0.082
Balanced, endo- and mesomorphy	15	——	——	——
Balanced, meso- and ectomorphy	19	0.028	0.872	+ 0.155
Balanced, all 3 components	26	0.026	0.968	— 0.033

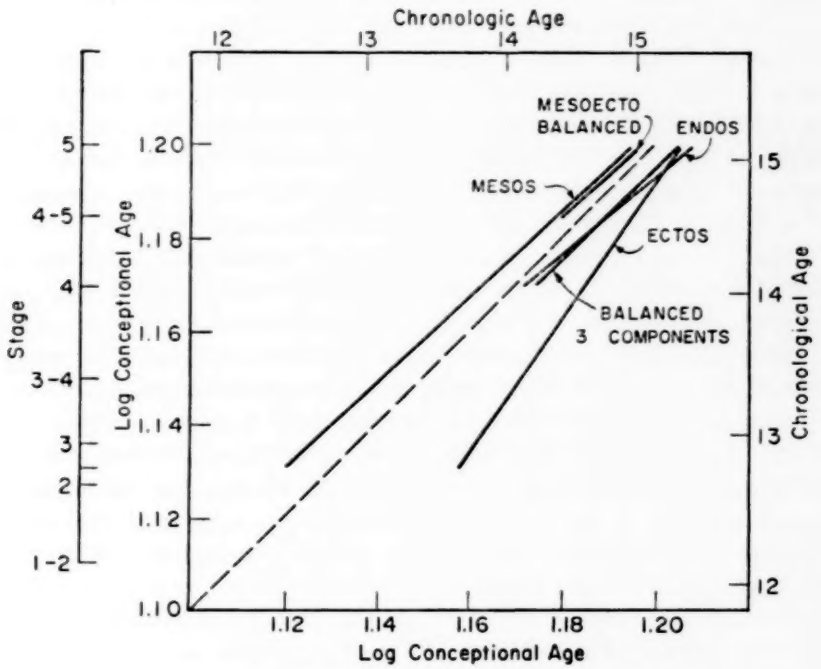

FIG. 3. DEVELOPMENT OF SOMATOTYPE CLASSES.

(endomorphs) are the most variable. This finding agrees with the clinical observation that deviant chronologies of sexual maturation are most often found in obese adolescents of both sexes.

Like variability, the *velocity* of sexual maturation seems to have a relationship to the fat content of the body, but in an unexpected direction. Although the endomorphic sample is small enough to be somewhat suspect, it appears that the slowest maturation occurs in the fattest boys. The velocity is definitely fastest in the leanest sample. The other groups do not deviate much from the average velocity.

Because of his slowness of development, the average endomorph begins sexual maturation early, but completes the sequence of stages late. Because of his very rapid development, on the other hand, the typical ectomorph is more retarded at pubescence than later on.

DISCUSSION

Mesomorphy is easy to see in the external form of the body—especially in males—as the outlines of muscles and usually a relatively masculine appearance. Boys with considerable mesomorphy appear to have an early but rather variable onset of pubescence, and to proceed at about the average velocity through their later stages of sexual development. One can speculate as to whether the tissues of the mesomorphic body respond early and fully, but not rapidly, to androgens, since many of its features appear to exaggerate the ordinary physiologic response to these hormones —particularly the coarse skin and prominent muscles.

Many observers have noted that caloric nutriture may hasten or retard the maturation of the mammalian body (Tanner, '55). In our opinion, caloric balance is important in influencing the time of *onset* of sexual maturation. If a boy consumes more calories than he needs, he will grow fatter and in so doing may reach pubescence sooner.

Caloric nutriture, as reflected in total body fat, also seems to influence the *velocity* of sexual maturation, but in a manner different from its effects on the beginning of pubescence. The progress of the maturational stages is at least partially controlled by androgens and other hormones. Once the transformation has started, it appears that the rising titers of these hormones produce an intense response, or rapid maturation, in the lean individual. This reaction is rather reminiscent of the physiological response to stimulant drugs in ectomorphs.

Since the steroid hormones are fat-soluble, one wonders whether they are stored or metabolized in the excess adipose tissue of fat boys, and

are thereby prevented from exerting their full effects on the maturing genitalia and sexual hair.

These conjectures emphasize the desirability of further research—especially on a longitudinal basis—on body composition, the titers of endocrine secretions in body fluids, and rates of maturation in adolescents of both sexes. Another desirable project would be to learn how fat animals differ from lean ones in their sensitivity to steroid hormones, as well as in their transport, storage and metabolism of these substances.

SUMMARY

Where stages of maturation have been defined and applied to a sample of children, it is convenient to record the percentages of individuals who are at or beyond a stage as related to their ages. Such distributions may be transformed into a so-called "attainment curve." If grouped data are available, a convenient method is to plot the percentages on log probability paper. In this case, age is transformed into the logarithm of conceptional age, and the percentages of individuals into standard scores around a zero point at which 50% of the population are at or beyond the given stage.

In studies of both dental development and sexual maturation, attainment curves on log probability paper form straight parallel lines. For stringent theoretical reasons, a succession of attainment curves for stages of development within one organ tend to be parallel. Tests of parallelism between different organs are valuable indications of their systematic or integrated relationships with one another.

This method of recording the chronology of developmental stages has versatility and generality. It can conveniently be attempted whenever data are available on children of various ages and degrees of maturation. With little computational effort, the method can provide an abundance of information such as the variability of the group in attaining its stages of development, a developmental age equivalent for each stage, and at any desired age, the incidence of children in the population who are within each stage.

A crude method was devised of computing the equations of parallel attainment curves. This procedure was applied to the stages of sexual maturation which had been recorded in 226 boys at a New England boarding school. These students had also been somatotyped. A study was therefore carried out which related body build and the trajectories of sexual maturation in these boys. For each of 5 somatotype subgroups,

we calculated the variability of attaining the stages. Allometric equations relating most of the subgroups to the total series revealed the timing and velocity of maturation in boys of different physiques.

Our data agreed with the findings of many previous authors that mesomorphy is associated with early maturation. In predominantly mesomorphic boys, the attainment of the stages is slightly more variable that the average, and the velocity of maturation is about average.

The association of ectomorphy with late maturation has long been known. In our group, ectomorphs show a small variability in the ages of attainment of the stages, but their velocity is 44% faster than the average. This rapidity of development is suggestive of a physiologic over-response to the increasing production of androgens and other trophic hormones which occurs in adolescence.

Although the endomorphic sample is small, it shows high variability in the ages of attainment of the stages, an early onset and late ending of sexual maturation. The velocity is therefore low.

Possible relationships between these findings and nutriture and body composition are discussed.

ACKNOWLEDGMENTS

The original study of the school population was supported financially by the Carnegie Corporation, and the present analyses were carried out in part with the support of The Grant Foundation, Inc. The methodology and machine computations were developed during the senior author's tenure of a Fulbright Visiting Lecturership at the University of Melbourne, Australia.

The authors especially wish to acknowledge the help of C. W. Dupertuis and W. W. Greulich, whose ratings of physique and maturation are the basis of the entire investigation. Others who have contributed much to this project have been A. F. Roche of the Department of Anatomy, Melbourne; R. C. Reed and J. Mayer of the Harvard School of Public Health; and W. W. Howells of the Harvard Department of Anthropology.

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BOOK REVIEWS

Modern Ideas on Spontaneous Generation. Edited by R. F. NIGRELLI. 121 pp. Ann. N. Y. Acad. Sci. *69*, Art. 2. N. Y., 1957. $2.50.

If the title of this symposium seems startling to the reader, let us admit that it also seems so to the reviewer and evidently even to some of the contributors. Blum, in his introductory remarks, mentions that the term "spontaneous generation" was taboo among biologists only a few years ago. Of course the modern use of the term has little in common with the ancient pictures of flies arising spontaneously from dead animals and frogs from mud. This is not happening now, and never did. It may be that even the simplest living molecules cannot arise now from non-living material. But H. F. Blum points out that our concepts of evolution and the biochemical evidence we now have seem to require us to believe that, at some time in the past, life did emerge from a non-living milieu.

One of the conclusions forced on the reader is that earlier speculations on the origin of life and the nature of the earliest living molecules are now being taken more seriously than when first proposed. This reviewer bought one of the first copies of the English translation of Oparin's pioneer work. He cannot remember ever discussing it with a scientist who took it seriously. Oparin's ideas seem to be the basis for modern thinking on the subject, and S. L. Miller gives in his chapter of the Symposium an account of his now classic experiments in which he successfully tested experimentally the ideas of Urey and Oparin that organic molecules such as amino acids might originate spontaneously in a reducing atmosphere such as that of the earth in its early stages.

From amino acids to proteins is in theory but a step; the actual sequence of events is still unknown. S. Granick suggests that the first organization of preprotoplasm would be a primitive energy-conversion unit, originating from some common minerals containing metal ions serving as coordinating templates and catalysts, which could perform the elementary process of photosynthesis and respiration. Granick presents interesting suggestions as to the origin of enzymes from inorganic ions by successive complexing with organic compounds.

G. Wald contributes a fascinating discussion of the origin of optical

activity, including an apparently original suggestion that from the unit molecules provided by geochemical processes in racemic mixtures, single optical isomers were selected in the process of composing structures of higher order: polypeptides and proteins from amino acids, nucleic acids from nucleotides, etc.

This symposium does not reflect particularly the growing conviction of many investigators that nucleic acid is the primary stuff of heredity and therefore of life, and C. C. Lindegren in his chapter points out the inadequacy of destruction of transforming principles by DNAase to prove that the gene is composed exclusively of DNA.

Space does not permit a summary of the other contributions: S. H. Hutner and others write on "Electrolyte requirements of protists and archeometabolism," A. Gulick on "Phosphorus and the origin of life," R. C. Warner on "The interaction of synthetic polynucleotides," D. Harker on "The structure of crystalline proteins," S. W. Fox and others on "Spontaneous generation of anabolic pathways, protein, and nucleic acid," and N. W. Pirie on "Some assumptions underlying discussions on the origins of life." P. H. Abelson contributes a chapter on "Some aspects of paleobiochemistry" which was of particular interest to the reviewer.

This timely monograph will be of value to all interested in the matter, although as is to be expected from the present state of our knowledge, it is thought-provoking and suggestive rather than definitive or comprehensive.

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Chemical Anthropology: a New Approach to Growth in Children. By ICIE G. MACY and H. J. KELLY. xi + 149 pp. University of Chicago Press, 1957. $3.75.

From 1942 to 1951, Drs. Macy and Kelly published three admirable volumes entitled *Nutrition and Chemical Growth in Childhood.* The present work, *Chemical Anthropology,* is a brief epitome of these earlier studies, with the added aim of calculating age trends in the body composition of children. These trends will be the major topic discussed here.

All four of these books are based on a semi-longitudinal nutritional balance study of healty preadolescent children who resided at the Methodist Children's Village, Detroit. It is still a model of excellence in its field, even though the data were gathered some twenty years ago. Because of its date of inception, hardly any of the modern techniques in the measurement of body composition were used. Instead, Drs. Macy and Kelly have had to use, and sometimes to devise, equations for predicting body constituents from anthropometric data. Some of the trends so obtained have already been published in Human Biol., *28* (*3*) : 289-308. Other constituents which could not be calculated from these anthropometric equations were arrived at by subtraction.

Underlying much of this work is the assumption that the mature percentages of chemical constituents of the human fat-free body are arrived at early in childhood. For a century, it has been known that the fetal organism contains a higher concentration of water than that of the adult. In 1923, Moulton estimated that mature hydration, which is the minimal adult water content of the human fat-free body, is attained in the interval from 500 to 1000 days post conception (J. Biol. Chem., *57*: 79-97). Macy and Kelly accept this formulation on the grounds that from the postnatal ages of 4 to 9 years, dimensional growth is relatively orderly and predictable in most children, and the increments of growth per unit of time are also fairly constant. To Macy and Kelly, this linear growth rate is an indication of a stable and even mature chemical composition of the fat-free body.

Logically enough, this interval of linear growth is the straightest portion of a curve of average measurements of a child population as plotted against chronological age. Since this linear interval occurs in many organisms besides man, we may learn from lower forms when this interval takes place relative to the attainment of chemical maturity. The data of Spray and Widdowson (Brit. J. Nutrition, *4*: 332-353) enable us to draw such conclusions from growth curves of body weight and carcass analyses of the rat, rabbit, cat and pig. In all of these species, mature hydration—and chemical maturity in general—are reached *at or after* the end of the interval of linear growth in weight.

Two lines of evidence suggest a similar situation in man. In the laboratory of the late Professor T. Wingate Todd, Venar measured the fresh wet weight and dry weight of children's skeletons. He found that the mature or minimal hydration of the skeleton was not reached until 12 years of age, but felt uncertain about his findings in view of Moulton's

much earlier estimates of the age of mature hydration of the fat-free body (p. 92, Part II, White House Conference on Child Health and Protection).

This reviewer and E. Giles calculated the allometry of water and fat-free solids in human fetal and neonatal carcasses, and projected these trends into childhood (Human Biol., *28* (*2*): 253-273). Our estimates of the minimal ages of mature hydration were about 10½ years in girls, and 14 years in boys. These estimates agree quite well with Venar's.

In *Chemical Anthropology,* prediction equations have been taken from the work of Friis-Hansen and his associates (Pediatrics, 7: 321-327) to arrive at total body water from body weight and from surface area. Drs. Macy and Kelly have computed their own equations for thiocyanate space from stature, weight and surface area, based on data from Morse *et al.* (Am. J. Physiol., *151*: 438-447). The values for total body water are of course close to those based on the equation of Hunt and Giles, which also comes from the Friis-Hansen study.

Accepting Moulton's early age of mature hydration, Macy and Kelly utilize a constant water-solids ratio. Since total body water falls from 57% of body weight at 4-6 years to 53% at 10-12, fat content must increase from 22% to 28% in the Detroit boys. If on the other hand the fat-free body continued to "solidify" during this span of growth, fat would be the constant constituent during the linear interval of growth.

It is difficult to reconcile an increasing fat content in preadolescent boys with the decreasing adiposity of the brachium (Baker, Hunt and Sen, Am. J. Phys. Anthrop., in press). Furthermore, studies of body density, total body water, and radiographs and skinfolds of adolescent boys agree that adolescent boys after the age of 12 years are far less adipose than the 28% which Macy and Kelly assign to the 10-12-year-old Detroit group. (Heald, Hunt *et al.*, in preparation).

Aside from these unresolved problems in the growth of body composition in children, *Chemical Anthropology* presents a wealth of material on the nutrition of the young which is of great value.

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Discussions on Child Development. Edited by J. M. TANNER and BÄRBEL INHELDER. Vol. I and II. The Proceedings of the first and second meetings of the World Health Organization Study Group on the psychological development of the child, Geneva, 1953. Tavistock Publications, London, 1956. 240 and 271 pp. Set of 2 vols. $10.00.

Edited verbatim reports of discussions between experts are becoming increasingly common. Eminent examples are the Macy Foundation Symposia and the Ross Pediatric Research Conferences. The organizers of such conferences do an *invaluable* job in bringing together the experts (usually from far and wide) and the idea to bring the reader into the discussion chamber is appealing. After a two-page stimulating presentation by an expert I find myself getting really interested and then one of two things happen: I either say (I whisper to an imaginary colleague), "I wonder what X will say to *that*?" and then X doesn't say it, and I am frustrated. Or when I hope that the speaker will go on and develop his ideas further, someone interrupts and says, "Do you mean, Doctor Y, that you are not in agreement with so and so?" Of course, this is just what did happen, and does happen in informal symposia; and nothing could be more admirable for a whole new train of discussion ensues. But, to read it in print is confusing and I am wondering whether such transactions merit formal publication.

The present two volumes are the result of the World Health Organization's bringing together twelve experts to discuss the biological, psychological, and cultural factors acting on childhood development and formation of the adult personality. In Volume I, Tanner contributes a foundation on somatic growth; Inhelder leads a discussion on the principles of Piaget (present) and Wallon regarding criteria of mental development; Zazzo and Bowlby present discussions on stages of psychological development and psychoanalytic instinct theory. Two papers (sparsely interrupted) by Grey-Walter on cerebral electro-genesis, and Lorenz on comparative behaviorology, with Mead's constant contributions on the application of anthropological techniques to the study of development, make this volume outstanding and important.

Volume II is devoted mainly to discussions on the mechanisms of learning in the human and animals, and to the social and moral aspects of behavior. The first presentation by Grey-Walter is devoted to the fascinating and important (and to me, rather frightening) electronic

tortoise, while Bindra, Liddell and Whiting present other headings for discussion. Discussions on films shown by Bowlby and Lorenz also are recorded.

This account does not do justice to the wealth of material found running through these volumes which represent about one-third of the verbatim record. Condensation of such materials is difficult but I cannot imagine how the editors' job could possibly be improved upon.

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The Human Brain. From Primitive to Modern. By A. M. LASSEK. vii + 242 pp. C. C. Thomas, Springfield, Ill. $4.75.

Arthur Lassek, Professor of Anatomy at Boston University School of Medicine and a principal authority on the structure of the pyramidal system, appears to have a dual purpose in *The Human Brain.* Much of the material is a popular account of neural structure. This is accurate and factual, affording captious critics only a few openings, such as the table on page 31 which gives the maximum weight of the male brain as 2000 and the minimum weight of the female as 800 gms.; figures uncorrected for age and body size are misleading. Lassek's purpose is not, however, mere description but "to portray the significance and impact of the long, past environment upon . . . the humain brain, and what it may mean to us. . . ." For such a purpose a much wider field of knowledge than is encompassed by anatomy must be examined, especially as Lassek desires to "make man more understandable and easier to deal with."

Periodically Lassek reminds the reader that "The outstanding fact in the evolution of man is the development of his mind"—the physical substrate of which is implied to be the brain—but as one progresses one finds the same old difficulties turning up. These are trouble in (1) defining exactly what the structural evolutionary advances are, (2) whether the process of structural evolution (as distinct from mere variation) is still continuing or whether it stopped 500,000 years B. C. (*i. e.* with the commencement of cultural evolution) and (3), if it is going on, whether there is any real correlation between it and those inspiring aspects of intellectual development which capture our imagination.

Lassek plays upon the familiar theme of structural difference between *Homo sapiens* and subhuman primates but quietly slips past the troublesome lack of information on the Pleistocene anthropoids. Everyone admits that the nervous system of man and monkey differ and that among these differences is hidden an interesting story. Still, the differences which exist have not been correlated with any specific function not only for the reason that present day average man rides the crest of a wave of culture, which buoys him far beyond his individual capacity of attainment, but also because we have only the most general idea of what the nervous system looked like in the Pleistocene anthropoids or how it functioned.

Once Lassek has assured us that the brain of *Homo sapiens* is in fact different from that of infrahuman primates he catalogues these differences and uniformly comes to the decision that whatever has happened has led to progress or has been immaterial. A greater development of the parietal lobe leads to manual activity and toolmaking we are told but the obvious degradation in the acuity of audition has, according to Lassek, led to the development of cerebral speech. From a consideration of structure Lassek moves directly into an exposition of the psychological aspects of human progress in the historical period. The implication is, of course, that the discussed differences between man and monkey are responsible for that progress. That these two sets of data are separated both in place and time is not clearly revealed and no material is brought forward to lead me to consider the necessity of changing the statement I made in print last year (Mettler, Fred A. 1956 *Culture and the Structural Evolution of the Neural System.* N. Y. The American Museum of Natural History), notably, that " there is no good evidence to support the assumption that man's neural system has undergone any progressive alteration in the direction of greater size or complexity since the middle of the Pleistocene."

Over half of the book is concerned with the psychological aspects of human progress noted above or, as Lassek calls it, the " Evolution of Mind." The " presavage mind," according to the author, was structurally subhuman and functionally acultural. The " savage mind " is identified with a period in which man " relied solely on hunting and fishing." " It can," Lassek says, " be taken for granted that there was a considerable increase in the magnitude of the human brain between the presavage (animal-man) and savage stages." Initial recognition of the ego he places in the savage period. He appears to regard this as a rather abrupt

event, likening it to the stroke of a gong. "With this realization, the first mental gong had struck in man's evolutionary time-clock and he was one step away from the mere reflex and animal stage."

The comparative psychologist, uncommitted to the proposition that the ego must, by definition, be a human characteristic and aware of the strong possessive behavior of animal forms, may find it difficult to accept the implication that the development of ego awareness is not a gradual and variable affair. The circumstances and events Lassek has envisioned do not appear to be entirely in accordance with available data or at least lack universal applicability. In his handling of the literature outside his own area of specialization there is some evidence that the author has fallen into the familiar error of giving uncritical acceptance to material of unequal merit and credence to outmoded and questionable sources.

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Behavior Theory and Conditioning. By KENNETH W. SPENCE. vii + 262 pp. Yale University Press, 1956. $4.50.

The non-specialist who happens onto this volume of the Silliman Lectures may well wonder what subject matter they represent. The title suggests something to do with physiology or psychology. Of these, the former is quickly disposed of. The term "conditioning" betrays a link with Pavlov. But whereas for Pavlov the theory of conditioning was nothing but physiology, for Spence it is anything but physiology. On the other hand, there is no mention of ink blots, IQ tests, or even tranquilizers. The talk is all of habit strength and reinforcement; of eyelid reflexes and rats in mazes; of exponential curves and probability integrals. The non-specialist must be assured that all this is indeed psychology, remote though it may seem from the everyday problems of teaching Johnny to read, improving Johnny's personality, or selling Johnny's parents new automobiles.

To understand Spence's book at all, one must realize that it has nothing immediately to do with man's practical problems. Spence makes it clear in his introductory lecture that he and his students have spent years recording eye blinks and observing maze runs with the sole purpose

of finding out how various measurements that can be made upon eye blinks and maze runs are influenced by factors in the person's or animal's environment. If there were only a few possible measurements and only a few determining conditions, the outcome of the researches could be summarized in a table and the job would be done. However, there turn out to be many measures, each depending upon many conditions. Consequently, if one shares with Spence a desire to make detailed predictions about how simple responses are learned, to give exact quantitative answers to questions about how the speed or magnitude or probability of a response will be affected by a change in this or that environmental condition, then one must have a theory.

The theory presented by Spence falls squarely in the main line of descent from the doctrines of associationism and conditioned reflexology that have been largely identified with learning theory in this country for several generations. Luckily for the reader, Spence has achieved theoretical progress by simplifying, rather than extending, the elaborate system within which Clark Hull attempted to comprehend the laws of learning. But the tactical streamlining of Hull's program is accompanied by little change in strategy. Order and economy are introduced into the proliferation of experimental laws by two main devices. Firstly, the tendency for any given stimulus to evoke a particular response is represented by a theoretical variable (" intervening variable ") termed reaction potential. Given the current value of the reaction potential, the axioms of the theory should generate predictions concerning the probability, latency, and other more or less directly measurable attributes of the response. Secondly, the determining conditions are grouped into three main classes: those having to do with frequency of past stimulus-response occurrences, with incentive conditions, and with motivating conditions. The basic laws of the theory relate changes in reaction potential to each of these classes of determiners. The bulk of Spence's book is devoted to summarizing previously existing evidence for the particular laws that he has chosen as axioms and to describing many new experiments which serve both to test the laws and to extend our predictive command over simple conditioning situations.

The Silliman Lectures at Yale University have traditionally represented attempts to acquaint a wide scientific audience with technical developments in particular disciplines. Like its predecessors, this volume will require some work on the part of the non-specialist reader but will probably more than repay the effort. And, although less directly, readers

of systematic biology, psychiatry, cybernetics, sociology, and perhaps even educational psychology for years to come will owe Spence a heavy debt if his lectures can somehow be forced to the attention of the many writers in those fields who still regard the doctrines of Pavlov and Thorndike as the last word in psychological theory.

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BOOK NOTICES

PHILOSOPHY OF SCIENCE. By Gustav Bergman. xiii + 181 pp. The University of Wisconsin Press, Madison, 1957. $4.75. A chapter, grown into a book, that was initially conceived as introduction to a volume on the logical analysis of psychology. The book retains its orientation toward the behavioral sciences.

AN INTRODUCTION TO THE STUDY OF EXPERIMENTAL MEDICINE. By Claude Bernard. xix + 226 pp. Dover, New York, 1957. $1.50. A new edition of the classical treatise. The work is worth re-reading and re-thinking in 1958, 93 years after its publication. An informative foreword was provided by Professor I. Bernard Cohen.

TEXTBOOK OF HUMAN ANATOMY. By J. D. Boyd, W. E. Le Gros Clark, W. J. Hamilton, J. M. Yoffey, S. Zuckerman and A. B. Appleton. xii + 1022 pp. Macmillan, New York, 1957. $16.50. A new, collaborative textbook motivated by the need 1) to present only the more relevant topographical details, 2) to emphasize the correlation between structure and function, and 3) not to neglect the fact that anatomy is an independent branch of biological science with problems and achievements of its own.

THE IMPORTANCE OF OVERWEIGHT. By Hilde Bruch. x + 438 pp. W. W. Norton, New York, 1957. $5.95. Eating more and exercising less inexorably leads to increase of weight through fat accumulation, but campaigns against obesity "are apt to overlook individual differences and may create more tension for those people who need to overeat as a means of combating anxiety, for self-assertion, or as compensation for unfulfilled ambitions" (p. 58).

REPORT ON THE WORLD SOCIAL SITUATION. By the Bureau of Social Affairs, United Nations Secretariat. vii + 198 pp. Columbia University Press, New York, 1957. $1.75. The *Report*, prepared in cooperation with several agencies of the United Nations (ILO, UNESCO, FAO, WHO), surveys the world population trends, health conditions, food and nutrition, education and conditions of work and employment. The second part deals with problems of urbanization.

AGEING IN INDUSTRY. By F. Le Gros Clark and Agnes C. Dunne. vi + 146 pp. The Philosophical Library, New York, 1956. $7.50. An inquiry, made in Great Britain and based on figures derived from census reports (1921, 1931, 1951), into the employment of older (65 +) male workers in modern industry.

PSYCHOLOGICAL TESTS AND PERSONNEL DECISIONS. By Lee J. Cronbach and Goldine C. Gleser. 165 pp. University of Illinois Press, Urbana, 1957. $3.50. A stimulating, original, technical contribution to the test theory, evolved from a systematic examination of the decision problems for which tests are used, with implications for biological study of individual differences.

PRINCIPLES OF IMMUNOLOGY. By J. E. Cushing and D. H. Campbell. ix + 344 pp. McGraw Hill, New York, 1957. $6.50. Written for graduate students and college seniors majoring in biology. As pointed out by E. A. Kabat in the Foreword, "immunology and immunochemistry, with powerful techniques for recognizing differences among proteins and polysaccharides, provides a tool of enormous versatility for the study of living systems."

THE VISUAL PIGMENTS. By H. J. A. Dartnall. vii + 216 pp. John Wiley, New York, 1957. $6.00. Describes in detail the physical and chemical properties of the photosensitive substances, extractable from the rod-cone layer of retinae, and the methods used to determine these properties.

NONPARAMETRIC METHODS IN STATISTICS. By D. A. S. Fraser. x + 299 pp. John Wiley, New York, 1957. $8.50. Nonparametric methods, many of them of recent origin, are concerned with standard problems, replacing the familiar assumption of normality by general assumptions concerning the distributions. The treatise is intended as a textbook for advanced courses in mathematical statistics.

THE EVOLUTION OF HUMAN NATURE. By C. Judson Herrick. x + 506 pp. University of Texas Press, Austin, 1956. $7.50. This impressive treatise on "psychobiology" grew out of 60 years of intensive and productive study of comparative anatomy of the nervous system, supplemented by wide reading on human behavior and its biological origins.

HYPOTHALAMUS UND THALAMUS. By W. R. Hess. 70 pp. Georg Thieme, Stuttgart, 1956. DM 36. The Atlas, with German and English legends, constitutes the third volume of the author's outstanding contributions to the *Physiology of the Brain Stem*.

CALCIUM METABOLISM. By J. T. Irving. xi + 177 pp. John Wiley, New York, 1957. $2.75. The monograph considers different facets of the problem (ingestion, absorption, utilization, retention, and excretion), including the calcium content of the human body.

NEBRASKA SYMPOSIUM ON MOTIVATION. Edited by Marshall R. Jones. xii + 430 pp. University of Nebraska Press, Lincoln, 1957. The fifth volume in the important series *Current Theory and Research in Motivation*, with topics ranging from physiological mechanisms of motivation to motivational dynamics of language behavior.

AN INTRODUCTION TO GENETIC STATISTICS. By Oscar Kempthorne. xvii + 545 pp. John Wiley, New York, 1957. $12.75. A successful "attempt to present the basic statistical concepts and tools which the genetic research worker needs, with examples from genetics." The detailed presentation of statistical techniques for the study of quantitative inheritance is an outstanding feature.

HUMAN BLOOD GROUPS AND INHERITANCE. By Sylvia D. Lawler and L. J. Lawler. viii + 103 pp. Harvard University Press, Cambridge, 1957. $1.50. A concise presentation, intelligible to the biology student and interested lay reader, of the subject. A chapter is devoted to a historical survey and to the significance of blood groups for human biology.

PREHISTORIC MAN. By André Leroi-Gourham. ix + 119 pp. Philosophical Library, New York, 1957. $4.75. A popular, readable account.

FEAR: CONTAGION AND CONQUEST. By James Clark Moloney. xii + 140 pp. Philosophical Library, New York, 1957. $3.75. Psychoanalyst's cross-cultural approach to the social and medical significance of fear and rage, with considerations of "experimental anthropology," focussed on contrasting the natives of Okinawa (motherly mothering) and Hawaiian Okinawans (transmission of tensions).

BIOGRAPHICAL MEMOIRS, Vol. XXX. By National Academy of Sciences. 409 pp. Columbia University Press, New York, 1957. $5.00. The volume contains, among others, the biographies of John Dewey (elected to the N. A. S. as a psychologist in 1910), biologist F. R. Lillie, and the psychologist L. L. Thurstone (*Multiple Factor Analysis*, 1947).

WOMANPOWER. By National Manpower Council. xxviii + 371 pp. Columbia University Press, New York, 1957. $5.00. The volume is introduced by a Summary of Recommendations (pp. 3-6) and a Statement by the National Manpower Council (pp. 7-39). Twelve chapters by the Council's staff on women as members of the labor force follow.

THE MEASUREMENT OF MEANING. By Charles E. Osgood, George J. Suci and Percy H. Tannenbaum. 342 pp. University of Illinois Press, Urbana, 1957. $7.50. A well documented "progress report" concerned with the development of objective measures of *meaning*, an important variable in human behavior.

A NATURAL SCIENCE OF SOCIETY. By A. R. Radcliffe-Brown. xii + 156 pp. The Free Press, Glencoe, 1957. $3.50. Transcript of a provocative seminar given in the Social Science Division of the University of Chicago some 20 years ago (1937), concerned with the possibility and prerequisites of a natural science of human societies.

PSYCHOLOGY IN THE SOVIET UNION. Edited by Brian Simon. vii + 305 pp. Stanford University Press, Stanford, 1957. $6.00. Welcome translations of 21 recent papers by Russian authors, introduced by Professor Smirnov's survey of psychological research carried out in 1953-55. The project grew out of a 1955 visit of a group of British educationists to the U. S. S. R.

A SHORT HISTORY OF ANATOMY & PHYSIOLOGY FROM THE GREEKS TO HARVEY. By Charles Singer. xii + 209 pp. Dover, New York, 1957. $1.75. A reprint, with minor adjustments, of a valuable work originally (1925) published under the title *The Evolution of Anatomy*. Richly illustrated.

THE PRINCIPLES OF HEREDITY. By L. H. Snyder and Paul R. David. xi + 507 pp. D. C. Heath, Boston, 1957. Fifth revised edition of a widely used textbook designed to acquaint the beginning student with the facts and general principles of inheritance. Examples from human genetics are considered throughout the text. There is a chapter on "The mutant gene in man" and on "Eugenics."

IVAN P. PAVLOV. By Harry K. Wells. 224 pp. International Publishers, New

York, 1956. $3.50. A philosopher's "attempt to introduce the reader to those teachings of Ivan P. Pavlov which are pertinent to the fields of psychology and psychiatry."

DEVELOPMENT OF VERTEBRATES. By Emil Witschi. xvi + 588 pp. W. B. Saunders, Philadelphia, 1956. $8.50. The text, designed for premedical students and zoology majors, presents the development of amphibians, fishes, birds, and mammals, including man (pp. 457-551). Profusely illustrated.

SOCIOLOGY IN THE UNITED STATES OF AMERICA. Edited by Hans L. Zetterberg. 156 pp. United Nations Educational, Scientific and Cultural Organization, Paris, 1956. $2.50. This collection of authoritative "trend reports" deals with methods and systematic theory, social groups and institutions (including sociology of knowledge and science), and some social problems (criminology, ethnic relations, mental health).

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